

The Effects of an Acute Bout of Whole-Body Vibration on Pulse Wave Velocity in Individuals with SCI

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Abstract

Cardiovascular disease is a leading cause of mortality in the spinal cord injured (SCI) population. Reduced arterial compliance is a cardiovascular risk factor and whole body vibration (WBV) has been shown to improve arterial compliance in able-bodied individuals. The study investigated the effect of an acute session of WBV on arterial compliance as measured by pulse wave velocity (PWV). On separate days, arm, leg and aortic PWV were measured pre- and post- a 45 minute session of passive stance (PS) and WBV. The WBV was intermittent with a set frequency of 45Hz and amplitude of 0.6mm. There was no condition by time effect when comparing PWV after WBV and PS. Following WBV, aortic (928.6 ± 127.7 vs. 901.1 ± 96.6 cm/sec), leg (1035.2 ± 113.8 vs. 1099.8 ± 114.2 cm/sec) and arm PWV (1118.9 ± 119.8 vs. 1181.1 ± 124.4 cm/s) did not change. As such, WBV did not reduce arterial compliance, however future research with protocol modifications is recommended.

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Chapter 1: Introduction

Sustaining a spinal cord injury (SCI) is a life-altering and devastating event. The prevalence of individuals living with a SCI in North America is approximately 1-2% of the total population. The main cause of SCI is motor vehicle accidents followed by falls, sport injuries and violence (DeVivo *et al.*, 1999; Pickett *et al.*, 2006). The average lifetime cost for individuals living in the United States with paraplegia and an age of injury of 25 years is \$428,000, and the average lifetime cost for individuals living with tetraplegia with an age of onset of 25 years is \$1.25 million (Gondim *et al.*, 2004).

With SCI, the most obvious life altering effect is the individual's loss of mobility. However, after sustaining a SCI there are many life-threatening secondary health consequences in both the acute and long-term stages of the disability. Acutely, pulmonary complications are the most common cause of death, while in the long-term, respiratory and cardiovascular complications account for half of all deaths (DeVivo *et al.*, 1999).

Cardiovascular disease (CVD) is becoming a leading cause of mortality among the SCI population and the morbidity associated with CVD is prominent at a younger age (Krassioukov *et al.*, 2003). With an increased survival rate within the SCI population, CVD will continue to increase and account for greater morbidity and mortality. Along with the altered autonomic function, the primary risk factors for CVD are the sedentary lifestyle and lack of physical activity associated with the injury (Groah *et al.*, 2001), which in turn lead to an increased risk of type 2 diabetes (Myers *et al.*, 2007), dyslipaemia (Bauman *et al.*, 1999; Jones *et al.*, 2004; Myers *et al.*, 2007), intramuscular fat (Bauman *et al.*, 1999; Elder *et al.*, 2004), and greater platelet aggregation (Kahn *et al.*, 2001).

Another significant risk factor for CVD is the reduction of arterial compliance; or the increase in the stiffness of the blood vessels. Diminished arterial compliance is associated with cardiovascular and coronary arterial events such as myocardial infarction (Nakae *et al.*, 2008), atherosclerosis (Arnett *et al.*, 1994), and an increase in systolic blood pressure (Arnett *et al.*, 1994; Hermeling *et al.*, 2007). As well, arterial stiffness promotes ventricular wall remodeling and subsequent load-dependent alterations in diastolic function (Abhayaratna *et al.*, 2008). Arterial compliance is, in part, a function of the change in the intimal-media layer of the arterial endothelium. A reduced ratio of elastin to collagen and/or an increased smooth muscle tone results in decreased compliance of the vessel. A lower degree of arterial compliance is associated with the cardiovascular risk factors of age, gender, lipoprotein abnormalities and diabetes (Arnett *et al.*, 1994).

Measures of arterial compliance are conducted by estimating the artery's capacity to expand and contract with cardiac pulsation and relaxation. Pulse wave velocity (PWV) refers to the speed of the blood pressure wave as it travels along a vessel, and the measurement of this velocity can be used as a non-invasive diagnostic tool for the estimate of arterial compliance. Specifically, PWV is the measurement of the speed of the blood pressure wave as it travels between two sets of anatomical points within the arterial system (Miyatani *et al.*, 2009). A faster speed of the blood pressure wave signifies a stiffer and less compliant blood vessel. The use of PWV as a non-invasive imaging technique may aid in quantifying the risk of CVD and in fact, this measurement technique, has been shown to predict cardiovascular outcomes independent of traditional risk factors (Abhayaratna *et al.*, 2008).

There are two measurement strategies used when evaluating PWV. The first concerns 'central' PWV which measures long arterial trajectories and is measured between the carotid and femoral arteries (Hermeling *et al.*, 2007). The second method concerns 'peripheral' PWV. In this method, the blood pressure wave is measured within a small arterial trajectory, for example from the femoral artery to the posterior tibial artery (Hermeling *et al.*, 2007). Central PWV, measured along the aortic and aortoiliac pathway, is most clinically relevant because the aorta and its first branches are responsible for most of the pathophysiological effects of reduced arterial compliance (Boutouyrie *et al.*, 2002).

One study known to date has investigated the use of PWV to assess arterial compliance for individuals living with SCI. Miyatani *et al.* (2009) compared a cohort of 12 individuals with SCI to age, gender, height and weight matched non-SCI controls. The study found that mean aortic (central) PWV was greater in the SCI group than the control group ($1274 \pm 369 \text{ cm/s}$ to $948 \pm 110 \text{ cm/s}$), suggesting an increased risk for CVD in the SCI group.

Pulse wave velocity has been shown to be a valid and reliable estimate of arterial stiffness in able-bodied individuals. Lehmann *et al.* (1992) determined the coefficient of variation (CV) of intra- (8.5%) and inter- (9.4%) observer repeatability to be very low for aortic PWV in healthy individuals. In addition, studies by Lee *et al.* (2009) and Naidu *et al.* (2005) used intraclass correlations to demonstrate significant high correlations ($p < 0.05$) for intra- and inter-observer reliability for aortic PWV measurements. However, Frimodt-Moller *et al.*, (2008) found a significant intra-observer difference for aortic PWV despite no significant inter-observer difference. There was also no difference found for

intra- or inter-observer brachial PWV (Frimodt-Moller *et al.*, 2008). Therefore, despite the demonstrated repeatability of PWV, it may still be necessary to conduct inter- and intra-observer repeatability calculations to ensure proper interpretation of results. As it has never been evaluated in the SCI population, future studies should determine the inter- and intra-observer reliability for PWV in this population.

Arterial compliance has been studied in conjunction with exercise protocols primarily focusing on aerobic and resistance training (Heffernan *et al.*, 2007; Otsuki *et al.*, 2007). These studies demonstrated that after endurance training, arterial compliance was increased while after strength training, arterial compliance was decreased. Similarly, Jae and colleagues (2008) found that individuals living with paraplegia who regularly participated in aerobic exercise had no difference in carotid mean intima thickness (another index of arterial compliance) when compared to able-bodied individuals. Likewise, normotensive paraplegics who did not participate in regular exercise, demonstrated decreased arterial compliance, as determined by augmentation index, when compared to able-bodied controls (Yim *et al.*, 1993).

Exercise is an important component of what is considered to be a healthy lifestyle and aerobic exercise has been shown to increase arterial compliance and improve cardiovascular health (Tanaka *et al.*, 2000; Thijssen *et al.*, 2007). Unfortunately, exercise can be difficult for those living with a SCI and as such, this population is living within the low end of the physical activity spectrum (Elder *et al.*, 2004). The most common modalities of exercise which significantly affect cardiovascular outcomes for individuals with a SCI include arm ergometry (Cowell *et al.*, 1986; Davis *et al.*, 1981; Franklin, 1985), body-weight supported treadmill training (BWSTT) (Ditor *et al.*, 2005) and

functional electrical stimulation (FES) (Mutton *et al.*, 1997). However, these exercise modalities have many disadvantages. Arm ergometry may only be beneficial for those with higher level functioning, thus excluding many individuals living with tetraplegia while BWSTT is very costly and labour intensive. FES carries the small but notable risks of pain, autonomic dysreflexia, and bone fractures and, cannot be used in individuals with lower motor neuron injuries.

Whole body vibration (WBV) may be a unique exercise solution for individuals with SCI. When standing on a platform which oscillates vertically or in a sinusoidal direction, the vibrations are transmitted through the body eliciting a stretch reflex in the muscles. This neuromuscular response is known as the 'tonic vibration reflex'. This reflex is able to cause an increase in recruitment of motor units through activation of muscle spindle and polysynaptic pathways (Seidel, 1988). As well, the effect of the vibration causing a mechanical shearing of the blood vessels is thought to result in vessel deformation and release of nitric oxide which causes vasodilatation. This form of exercise shows promise for vulnerable populations who have a limited ability to perform voluntary exercise.

In the able-bodied population, one study has investigated the direct effect of WBV on arterial compliance using PWV as the experimental measure. Otsuki and colleagues (2008) assessed arterial compliance measuring brachial-ankle PWV in 10 healthy men, before as well as 20, 40 and 60 minutes after acute bouts of WBV. Vibration was set at 26Hz and a 2-4mm amplitude. Vibration occurred for 10 sets of 60 seconds on, 60 seconds off. The results showed that in the WBV group, brachial-ankle PWV was significantly reduced at 20 and 40 minutes but not 60 minutes after the trial

without any significant decrease in blood pressure. The mechanisms underlying the exercise-induced acute reduction of arterial compliance is unknown but may be related to mechanical stimuli, which as mentioned, may elicit vasodilatation via the release of nitric oxide (Otsuki *et al.*, 2008).

The results of the studies mentioned show a great promise for the SCI population. Because individuals with SCI typically adopt a sedentary lifestyle, they are at increased risk for CVD and have an increased morbidity at a younger age compared to the able-bodied population. It is known that aerobic exercise improves cardiovascular fitness. However people with SCI, particularly individuals living with tetraplegia, face challenges finding effective exercise modalities. The modalities currently available (arm ergometry, FES, BWSTT) while beneficial to some individuals have side effects and/or complications and pose practical administrative problems. The use of WBV has been shown to augment arterial compliance in able-bodied individuals, who are either in good health or suffer from disease. It is possible that WBV will be an effective form of exercise to increase the arterial compliance in individuals with SCI and therefore improve their cardiovascular health.

This study will evaluate the change in arterial compliance following acute WBV exercise using the non-invasive measurement of PWV. If an increase in arterial compliance is observed, WBV may be further studied and protocols designed to provide a safe, practical and easily applied form of CVD risk reduction for individuals with SCI who have difficulty with traditional exercise. In addition, this study will evaluate the inter- and intra-observer reliability for PWV in individuals with SCI as it has previously never been done.

It is postulated that a reduction in arterial stiffness will improve cardiovascular health and reduce CVD morbidity, thus improving the quality of life and reducing the medical costs related to living with SCI. Reduced arterial compliance is associated with increased risk for CVD and coronary artery disease and therefore increasing compliance would ultimately reduce the risk and the associated morbidity and mortality.

1.1 Hypotheses

The hypotheses of the current study are: i) each participant will show a reduction in PWV after an acute bout of WBV similar to Otsuki *et al.* (2008) of approximately 3%; ii) individuals with incomplete injuries will show a greater reduction in PWV following WBV compared to individuals with complete injuries as they have the availability of increased muscle activation; and iii) individuals with injuries below T5 will show a greater reduction in PWV following WBV compared to those with injuries above T5 due to a lesser degree of autonomic dysfunction. As found within the able-bodied population, we believe that PWV will have high intra- and inter-observer reliability for individuals with SCI.

Chapter 2 - Review of the Literature

2.0 Epidemiology

2.0.1 Demographics

Sustaining a spinal cord injury (SCI) is a devastating and life-altering event. In the United States, there are 450,000 people living with a SCI or 1-2% of the population with a similar percentage found in Canada. In 1994, there were 10,000 new American cases and new cases were expected to rise to 13,400 per year by the year 2010 (Phillips *et al.*, 1998). In Canada, the annual incidence of SCI between 1997 and 2000 increased by greater than two-fold from approximately 21 individuals per million to 49 individuals per million (Pickett *et al.*, 2006). Males sustain the vast majority of injuries, accounting for 82% of all injuries. The majority of new injuries sustained occur between the ages of 16-30 with a median age of 26 and the most common age of injury is 19 (Phillips *et al.*, 1998). Males and younger adults are believed to sustain the vast majority of injuries due to their greater propensity for high-risk behaviour. In Canada, motor vehicle accidents account for the highest number of SCI at 35%, followed by falls at 31%, sport and recreation accidents at 13%, industrial accidents at 10%, and violence at 5% (DeVivo *et al.*, 1999; Pickett *et al.*, 2006). The cost of living with a SCI is very high. In the United States, the average first year expenses for individuals living with paraplegia amount to \$152,000 and first year expenses for individuals living with tetraplegia amount to \$417,000. The average lifetime cost for individuals living with paraplegia with an onset of injury at age 25 has been estimated at \$428,000 and the average lifetime cost for individuals living with tetraplegia with an onset of injury at age 25 has been estimated at \$1.35 million (Gondim *et al.*, 2004).

2.0.2 Classification of Spinal Cord Injuries

A SCI is classified with regard to both the level and severity of injury. If the neurological level of injury is C8 or above, then the individual is considered to be living with tetraplegia as the impairment or loss of motor and/or sensory function occurs in the upper and lower limbs, trunk and pelvic organs. An individual with a neurological level of injury of T1 or lower is considered to be living with paraplegia as the motor and sensory function is normal in the upper limbs.

Regarding injury severity, a SCI may be classified as complete or incomplete. A complete injury is defined as an injury with complete loss of all motor and sensory functions at the S4-S5 level. An incomplete injury results in some degree of preservation of motor and/or sensory function at the S4-S5 level and therefore individuals living with incomplete injuries have spared motor or sensory function below the level of the lesion. It is important to note that individuals living with a complete SCI may still have some sensory or motor function below the level of the lesion despite lacking motor or sensory function at S4-S5. This 'zone of partial preservation' typically extends a few segments below the lesion level, after which there is no sensory or motor function. Of all individuals living with SCI, approximately 18% are living with complete tetraplegia, 31% are living with incomplete tetraplegia, 28% are living with complete paraplegia and 23% are living with incomplete paraplegia (Phillips *et al.*, 1998).

A more precise classification of injury severity is offered by the American Spinal Injury Association (ASIA). In this classification, injuries are divided into 5 subdivisions,

A-E, gradually decreasing in severity. Refer to Appendix B for further detail regarding these classifications.

2.1 Cardiovascular Disease (CVD) and Dysfunction after Spinal Cord Injury

2.1.1 Cardiovascular Disease and Spinal Cord Injury

Perhaps the most striking effect of a SCI is the resulting immobility. However, a SCI also causes many life-threatening secondary consequences. Mortality is highest in the first year of injury, particularly for those with severe injuries. Factors that are considered for life expectancy include age, severity and level of injury as well as ventilator dependency (DeVivo *et al.*, 1999). Respiratory and heart related complications account for over half of all deaths associated with SCI (DeVivo *et al.*, 1999). However, with advancements in medicine and rehabilitation techniques, the life expectancy following an injury is increasing. As a result, individuals with SCI are becoming more prone to the typical age-related health risks and cardiovascular disease (CVD) is becoming a leading cause of mortality among the SCI population and the morbidity associated with CVD is more prominent at a younger age (Krassioukov *et al.*, 2003). With an increasing long-term survival within the SCI population, CVD will continue to increase and account for greater morbidity and mortality (Groah *et al.*, 2001).

2.1.2 Cardiovascular Dysfunction after SCI

Following a SCI of the upper thoracic or cervical levels, the sympathetic nervous system (SNS) is disrupted and this results in subsequent autonomic dysfunction. Cardiovascular control is abnormal and unstable after a SCI, and is often characterized by long-term low levels of sympathetic activity interspersed with episodes of reflex sympathetic hyperactivity (Krassioukov & Weaver, 1995). Furthermore, there is an

inability of supraspinal vasomotor centres to effectively respond to cardiovascular reflexes and altered vascular tone (Phillips *et al.*, 1998).

The heart is innervated by SNS fibres that originate at the T1-T4 level. The postganglionic SNS fibres release norepinephrine which then acts on the sinoatrial (SA) and atrioventricular (AV) nodes, the walls of the ventricles as well as blood vessel walls to increase heart rate and the force of ventricular contraction as well as vasoconstriction of blood vessels. The PNS, via the vagus nerve, slows the heart rate and force of contraction. Therefore, cervical injuries as well as high-level thoracic injuries result in a great deal of autonomic dysregulation as the signals being sent by the SNS are interrupted causing a loss of sympathetic tone resulting in hypotension and bradycardia (Teasell *et al.*, 2000) while at the same time, the signals sent by the PNS are uninhibited via the influence of the vagus nerve (Krassioukov *et al.*, 2007). In addition to the reduced levels of norepinephrine, there is a reduced sympathetic tone due to the reduced plasma epinephrine. This reduction in plasma epinephrine is due to an interruption of the sympathetic nerves in the spinal cord that send the efferent signals from the CNS to the adrenal medulla (Krassioukov *et al.*, 2007).

Importantly, the response of the cardiovascular system to exercise is affected by SCI. The SNS responds to exercise by causing a vasoconstriction at inactive muscles and the abdominal organs via the splanchnic nerves. Heart rate and contractility are also increased. These actions result in a greater venous return and end-diastolic volume and ultimately an increase in cardiac output. After a high level SCI, this sympathetic response is impaired, resulting in a reduced maximal cardiac output and consequent exercise

intolerance (Teasell *et al.*, 2000). Thus, rehabilitation strategies designed to reduce cardiovascular complications that do not employ traditional exercise are warranted.

2.1.2.1 Autonomic Dysreflexia

When prescribing exercise in this population, two important autonomic risks must be considered. The first is autonomic dysreflexia which is a potentially life-threatening phenomenon that affects 48-90% of individuals with SCI and is more common in those with an injury T6 and above (Bravo *et al.*, 2004; Myers *et al.*, 2007), although, it has been reported in individuals with injuries as low as T8-T10 (Teasell *et al.*, 2000).

Autonomic dysreflexia is a paroxysmal reflex of sympathetic activity in response to noxious or non-noxious stimuli below the lesion (Colachis & Clinchot, 1997). It is characterized by sympathetic hyperactivity below the level of injury causing moderate to severe vasoconstriction and hypertension with accompanying increases in stroke volume and cardiac output (Myers *et al.*, 2007). Stimuli triggering the response may range in severity from an otherwise non-threatening pressure below the injury or a distended bladder, to a broken bone in the lower limb.

Potential cardiovascular complications resulting from a bout of autonomic dysreflexia include left ventricular failure resulting in pulmonary edema, premature atrial and ventricular contractions, atrial fibrillation, tachycardia, myocardial ischemia and arrhythmias (Bravo *et al.*, 2004; Colachis & Clinchot, 1997). Autonomic dysreflexia puts the population at a significant risk for acute coronary syndrome and cerebrovascular accidents and is the fourth leading cause of death from secondary impairments (Krassioukov *et al.*, 2003). The cerebrovascular accidents include subarachnoid and intracranial hemorrhages and ischemic strokes.

Autonomic dysreflexia is caused by excessive peripheral responses to the release of catecholamines below the level of the lesion (Teasell *et al.*, 2000). In addition, a SCI leaves the sympathetic activity below the lesion functionally separated from the inhibitory effects of supraspinal regulatory centres. As a result there is a loss of sympathetic integration and sympathetic activity becomes reflexive and highly excitable (Bravo *et al.*, 2004). Vasomotor reflexes above the level of injury attempt to lower blood pressure by increasing parasympathetic stimulation to the heart via the vagus nerve which results in light headedness as well as vasodilatation and skin flushing above the lesion (Myers *et al.*, 2007).

2.1.2.2 Orthostatic Hypotension

The second autonomic risk associated with exercise in this population is orthostatic hypotension. Orthostatic hypotension is defined as a decrease in systolic blood pressure of 20mmHg or more and a decrease of 10mmHg in diastolic blood pressure, upon the movement from a more supine position to a more upright position (Claydon *et al.*, 2006). The decrease in blood pressure is associated with an increase in pulse rate as the individual assumes the upright position. The presence of orthostatic hypotension is greater among individuals with higher level and complete SCI (especially above T6) due to the inability to constrict the splanchnic blood vessels (Claydon *et al.*, 2006). Orthostatic hypotension may also result from the reduced pumping action of the skeletal muscles, which reduces the venous return to the heart. This in turn reduces stroke volume, cardiac output and blood pressure (Gondim *et al.*, 2004).

Orthostatic hypotension affects the individual's ability to participate in activities that provoke drops in blood pressure and as such, causes a reduction in quality of life. It

also affects activities of daily living and participation in rehabilitation programs, and causes a deficit in cognitive performance and an increase in fatigue (Gondim *et al.*, 2004).

Autonomic dysreflexia and orthostatic hypotension are autonomic dysfunctions that decrease the quality of life for individuals living with SCI. It is important to take precautions during activity and exercise to monitor and prevent the development of these dysfunctions from occurring.

2.3 Risk Factors Contributing to the Development of CVD

The high prevalence of CVD in the SCI population is caused by risk factors resulting from altered autonomic function as well as the sedentary lifestyle that arises due to the injury. Many of the risks associated with CVD in individuals with a SCI are similar to those of an untrained, able-bodied individual (Groah *et al.*, 2001). This illustrates the direct consequence of the sedentary lifestyle that is typically adopted post-injury on cardiovascular health. Altered autonomic function as previously mentioned, diminished physical exercise, altered lipid profiles and a reduced glucose tolerance are some of the risk factors of CVD in SCI (Groah *et al.*, 2001). As well, arterial stiffness has been described as an independent risk factor for CVD (Arnett *et al.*, 1994; Glasser *et al.*, 1997). Although this thesis is primarily concerned with arterial compliance after SCI, a brief discussion of all of the above risk factors is warranted, as they are interrelated in their detrimental effects on cardiovascular health.

2.3.1 Insulin Insensitivity

As a consequence of inactivity, the body fat percentage in the SCI population is 8-18% higher than age-matched, able-bodied individuals (Buchholz & Bugaresti, 2005). Intramuscular fat impedes glucose metabolism and is highly correlated with insulin insensitivity (Elder *et al.*, 2004). Elder and colleagues (2004) reported that SCI subjects with higher intramuscular fat also had higher glucose and insulin values after glucose ingestion during the oral glucose tolerance test than able-bodied individuals with a similar diagnosis of diabetes mellitus. However, these subjects with SCI also had a reduced muscle cross-sectional area, which in turn, influences glucose and insulin values following an oral glucose tolerance test. Therefore, high intramuscular fat in conjunction with a decrease in muscle cross sectional area worsens insulin insensitivity. Diabetes mellitus has been found to be high among the SCI population, with a prevalence of nearly 23% of the total population (Myers *et al.*, 2007). An individual with a SCI has a two-fold increase in the risk of cardiovascular mortality after being diagnosed with diabetes mellitus (Myers *et al.*, 2007).

2.3.2 Altered Lipid Profile

Dyslipaemia, a high antherogenic ratio of total cholesterol or low-density lipoprotein (LDL) to high-density lipoprotein (HDL), is another metabolic alteration that occurs with serious adverse effects. Individuals living with tetraplegia have a greater degree of dyslipaemia, in turn increasing their risk for CVD (Myers *et al.*, 2007). The dyslipaemia occurs as a result of high post-load insulin and low levels of physical activity. Serum levels of LDL have been shown to be very similar when comparing able-bodied and SCI subjects (Myers *et al.*, 2007). The increased dyslipaemia risk in the

SCI population lies in their reduced amount of serum HDL which is largely due to physical inactivity (Myers *et al.*, 2007).

HDL and LDL have a potent influence on the atherosclerotic process (Bauman *et al.*, 1999). LDL can penetrate the endothelial wall of a blood vessel and contribute to the creation of lipid foam cells, which form the core of a plaque deposit. When LDL is oxidized, it also triggers an inflammatory response within the endothelium accelerating the process of atherosclerosis. HDL is responsible for reversing the oxidation of LDL and as such, a high serum LDL coupled with a low serum HDL increases the risk of CVD (Bauman *et al.*, 1999). An increase in the cardiopulmonary fitness of an individual with SCI has been shown to positively influence the serum HDL cholesterol (Bauman *et al.*, 1999). Individuals living with tetraplegia who were regularly active in aerobic exercise as shown by a greater VO_2 peak (ml/min/kg) had a HDL level of 1.13mmol/L in comparison to the HDL level of 0.95mmol/L in sedentary individuals living with tetraplegia (Dallmeijer *et al.*, 1997).

2.3.3 Deep Vein Thrombosis

Deep vein thrombosis (DVT) is a major risk to the SCI population. A pulmonary embolus occurs when a thrombus detaches from a blood vessel and travels to the pulmonary arteries and blocks the blood flow to the lung; an event that is often fatal (Bravo *et al.*, 2004). While a DVT occurs in up to a third of individuals living with long-term SCI, the highest risk occurs acutely after the SCI. Acutely, 67-100% of these patients experience a DVT and consequently a pulmonary embolism is the third most common cause of death after SCI (Green *et al.*, 2003).

Individuals with SCI are more predisposed to thromboembolism due to the combination of peripheral venous stasis, intimal injury and platelet hypercoagulability (Kahn *et al.*, 2001). Venous stasis results from a lack of neurologic control in the vessels as well as in the voluntary muscles, as there is limited to absent muscle pump activity (Bravo *et al.*, 2004). A DVT occurs most often in the lower limbs. This can be attributed to vascular adaptations to inactivity and muscle atrophy, which considerably impair venous return from the lower extremities (Bravo *et al.*, 2004). Individuals with SCI have up to three times greater levels of platelet derived growth factor (PDGF), a known facilitator of platelet aggregation, than the able-bodied population and consequently have an increased risk for thrombus formation due to hypercoagulability (Kahn *et al.*, 2001).

2.3.4 Decreased Arterial Compliance

Arterial compliance is the ability of a blood vessel wall to expand and contract passively to an increase in volume when pressure changes occur. It is defined as the change in volume divided by the change in pressure. A decrease in arterial compliance is associated with many cardiovascular risk factors including age, gender, lipoprotein abnormalities and diabetes mellitus (Arnett *et al.*, 1994). Arterial compliance decreases with age and typically, women exhibit a lower arterial compliance than men beginning at a younger age (Noon *et al.*, 2008; Vermeersch *et al.*, 2008). Reduced arterial compliance is often associated with several disease states within the cardiovascular system such as isolated systolic hypertension, left ventricular hypertrophy, congestive heart failure and orthostatic hypotension (Tanaka *et al.*, 2000). A decreased level of arterial compliance is associated with coronary arterial events such as myocardial infarction (Nakae *et al.*, 2008), atherosclerosis (Arnett *et al.*, 1994) and an increase in systolic blood pressure

(Arnett *et al.*, 1994; Hermeling *et al.*, 2007).

The arterial system is designed as a network of vessels designed to convert the intermittent flow of blood from the heart to a continuous flow across the arterial tree, thus reducing the afterload imposed on the heart (Boreham *et al.*, 2004). Larger arteries instantaneously accommodate the volume of blood ejected from the heart and store part of the stroke volume during the systolic ejection, and via the elastic recoil of the muscular arterial vessels, drain the volume during diastole (Safar, 2001). Arterial compliance is reflected by the blood vessels' ability to expand and recoil with cardiac pulsation and relaxation (Tanaka *et al.*, 2000). Although blood flow is continuous, there is a pulse in blood vessels that is caused by a pressure wave that travels along the arteries. This wave is in response to the blood being pushed into the arteries during systole causing the arterial walls to expand. The compliance is a measure of the relationship between pressure and volume changes. In vessels with low compliance, a small increase in blood volume causes a large increase in blood pressure. Therefore as a vessel becomes less compliant, there is a greater rise in the pulse pressure (Kingwell, 2002). Compliance of the proximal aorta is the principal determinant of central pulse pressure. Larger arteries with decreased compliance cause the pulse pressure to rise due to higher systolic and lower diastolic pressure (Kingwell, 2002).

2.3.4.1 Effects of Decreased Compliance on the Cardiovascular System

Due to the decreased compliance caused by arterial stiffening, the arteries cannot adequately accommodate the volume ejected by the left ventricle (Hermeling *et al.*, 2007). The greater flow velocity attributed to the diminished arterial compliance causes wave reflections to return towards the aortic valve earlier in the cardiac cycle ultimately

arriving during the ejection phase causing the rise in systolic pressure (Abhayaratna *et al.*, 2008; Hermeling *et al.*, 2007). Thus, the same stroke volume will result in a higher pulse and systolic blood pressure. The increased afterload on the ventricle results in an increased myocardial oxygen demand and results in decreased oxygen supply to the heart (Boutouyrie *et al.*, 2002). The left ventricular hypertrophy and the elevation of systolic blood pressure ultimately lead to long-term raised left ventricular afterload and myocardial work. This results in a further reduction in coronary perfusion and thus leads to subendocardial ischaemia (Boutouyrie *et al.*, 2002).

2.3.4.2 Factors Determining Arterial Compliance

Arterial compliance is determined by structural and functional components and the intrinsic elastic properties of the artery (Arnett *et al.*, 1994). Structurally, the three layers and the lumen of the blood vessels affect arterial compliance. The innermost layer is the thinnest layer and is known as the *tunica intima*. It is composed of a single layer of simple squamous endothelial cells surrounded by a thin layer of subendothelial connective tissue interlaced with a number of circularly arranged elastic bands called internal elastic lamina. The outermost layer is known as the *tunica adventitia* and it is made entirely of connective tissue. The *tunica media* is the middle and thickest layer and has the greatest influence on arterial compliance. It is composed of circularly arranged elastic fibers, connective tissue and polysaccharide substances, and is separated from the inner layer by a thick elastic band known as the external elastic lamina. The innermost tissue of this layer is composed of elastic and smooth muscle that allows for the control vessel diameter. Elastin and collagen fibres compose the elastic tissue. When the artery is healthy, the proportion of elastin and collagen is held stable by a slow and dynamic

process of production and degradation (Zieman *et al.*, 2005). When this process is disrupted, there is vascular tissue dysregulation caused by stimulation of inflammatory molecules. This causes an overproduction of abnormal collagen and diminished quantities of normal elastin contributing to vascular stiffness and a decrease in compliance (Arnett *et al.*, 1994; Zieman *et al.*, 2005). As well, elevated smooth muscle tone or smooth muscle cell growth increases arterial stiffness (Arnett *et al.*, 1994).

Functional determinants of compliance are related to neurohumoral influences such as the renin-angiotensin system (RAS), (Glasser *et al.*, 1997). The RAS predominantly acts as a vasoconstrictor on arterioles. As well, this system has the ability to induce and elevate arterial stiffness by altering collagen and elastin thereby causing endothelial dysfunction by increased production of angiotensin II (Mahmud, 2004). Angiotensin II increases aortic pulse pressure without any noticeable changes to peripheral pulse pressure. Angiotensin II activity leads to collagen degradation, smooth muscle proliferation and the development of fibrosis which account for many of the underlying pathophysiological mechanisms that decrease arterial compliance (Mahmud, 2004). In a review by Zieman (2005) it was reported that diminished central arterial compliance and insulin resistance are positively correlated. Long-term hyperglycemia and hyperinsulineamia increase the local activity of the rennin-angiotensin-aldosterone system. This leads to the increased expression of the angiotensin type-1 receptor in vascular tissue. This increase in the angiotensin type-1 receptor is thought to initiate an inflammatory response promoting the development of wall hypertrophy and fibrosis leading to decreased arterial compliance.

Furthermore, reduced arterial compliance further increases the risk for

atherosclerosis. When the walls of the vessel are thickened, for any given blood volume flowing through the vessel, the smooth muscle cells are mechanically stretched more forcefully due to a greater pressure. This stretching of the smooth muscle cells results in an increase in collagen synthesis in the vessel wall further decreasing compliance (Arnett *et al.*, 1994) as well as causing arterial wall hyperreactivity (Laurent *et al.*, 2001). In addition, the forced stretching of the arterial wall augments the endothelial surface area. This increase in surface area causes an increase in intimal permeability to cohesive molecules such as albumin, lipoproteins and leukocytes ultimately leading to atherosclerotic plaque formations in the artery (Arnett *et al.*, 1994).

2.3.4.3 Arterial Compliance and Altered Lipid Profile

Noon and colleagues (2008) demonstrated that an increase in total cholesterol and LDL levels were associated with increases in both central and peripheral blood pressures. Elevated LDL levels were also associated with increased peripheral and central pulse pressures reflecting an increase in arterial stiffness. This can be attributed to endothelial dysfunction caused by the high levels of LDL.

2.3.4.4 Arterial Compliance and Diabetes Mellitus

As previously mentioned, the SCI population has a high prevalence of diabetes mellitus and type-2 diabetes has been discussed as a risk factor for CVD. Diabetes mellitus also has an influence on arterial compliance by causing endothelial dysfunction. It has been shown that elevated levels of plasma glucose cause connective tissue damage within the vessel (Glasser *et al.*, 1997). By affecting the connective tissue in an artery, the compliance is decreased as the vessel is no longer able to stretch the required amount in order to accommodate the blood being ejected through the artery.

2.3.4.5 Arterial Compliance and DVT

Although the direct relationship of arterial compliance and DVT has not been examined within the literature, a reasonable link can be made. With arterial stiffness, there is damage that is occurring to the vessel and further damage is likely during pulsatile changes in blood pressure. As the vessel is further damaged, the immune system attempts to repair it by greater platelet formation over the damaged area. With greater platelet formation and greater platelet aggregation in individuals with SCI as previously mentioned, there is a potentially increased risk of a thrombus being formed and dislodging from the vessel wall.

2.3.4.6 Arterial Compliance and Individuals living with SCI

Within the able-bodied population, diminished degrees of arterial compliance are associated with increased age, male gender, lipoprotein abnormalities, diabetes mellitus, obesity, lower physical activity levels and poor cardiovascular fitness (Miyatani *et al.*, 2009). Individuals living with SCI have lower physical activity levels and a resulting lower cardiovascular fitness (Phillips *et al.*, 1998).

Finally, people with SCI are at increased risk of pressure sore development due to poor tissue perfusion (Kanj *et al.*, 1998). Reduced arterial compliance in the peripheral vessels may reduce the blood flow to tissues supplied by the stiffer vessels.

Thus, reduced arterial compliance has important effects on the cardiovascular system and reducing the arterial stiffness may reverse the associated cardiovascular disease in the SCI population.

2.4 Assessment of Arterial Compliance

2.4.1 Augmentation Index and Carotid Intima-Media Thickness

Augmentation index (AI) and carotid intima-media thickness have been used to assess arterial compliance. AI can be considered a measurement of the functional component of arterial compliance. As the wave of the pulse pressure travels along the arterial tree, it encounters resistance in the arterioles of the periphery and the wave is subsequently reflected back to the heart. In healthy elastic arteries, the wave is reflected back during diastole. However, with a decrease in arterial compliance, the pulse pressure wave travels much more quickly along the arterial tree, thus arriving earlier in the cardiac cycle; specifically during systole. These early reflections in the aorta augment the systolic pressure so that the absolute systolic pressure is increased (Mahmud, 2004). Therefore in stiffer or less compliant vessels, there is a first systolic peak of pressure at ejection, plus a second peak resulting from the early reflective wave returning to the aorta before the end of systole (Mahmud, 2004). As such, the difference of the first peak and the second peak, due to the reflected wave, is the AI. Therefore, a higher AI results from reduced arterial compliance.

Carotid intima-medial thickness (CIMT) is a marker of structural vessel wall properties (Djaberi *et al.*, 2008). An increase in CIMT results in stiffening of a vessel and thus is a marker of reduced arterial compliance.

2.4.2 Pulse Wave Velocity

Pulse wave velocity (PWV) assessment is a topical detection method developed as a non-invasive diagnostic tool for the measurement of arterial compliance. As the ventricle ejects the stroke volume during systole the elastic properties of the arterial vessels expand with the increased pressure. During diastole, the ventricle relaxes and the

elastic walls of the vessels then recoil and move the blood volume forward creating a pulse. The change in the pressure between systole and diastole is the pulse pressure. The pulse travels along the arterial vessels as a wave of change of pressure. The speed of the wave is directly affected by the compliance of the vessels; a slower velocity being associated with greater compliance. PWV is an indirect evaluation of arterial compliance that is negatively correlated with arterial compliance; thus, the higher the PWV, the lower the arterial compliance and the stiffer the vessel. PWV has been shown to predict cardiovascular outcomes, independent of traditional risk factors (Abhayaratna *et al.*, 2008).

The methods of assessing arterial compliance such as AI, CMT and PWV are all accepted techniques. However, there is no direct comparison among the measurements. For example, there is no record of what level of AI will correlate with a particular PWV. Although this is the case, assumptions may be postulated regarding the various methods. As a higher AI is indicative of a pulse pressure wave reflecting back to the heart at a higher speed, it may be assumed that it is also correlated with a higher PWV. Similarly, increased CMT indicates increased vessel wall stiffness and therefore it may be associated with a faster pulse pressure wave velocity. Further research is required to establish meaningful links between these measurement techniques.

Taquet and colleagues (1993) found that PWV was directly associated with systolic and diastolic blood pressure. The association between high systolic blood pressure and a high PWV value may be related to the long-term increased blood pressure causing more forceful passive stretching of the collagen fibres of the blood vessel walls. This increased mechanical stretch will cause an increased production of collagen fibres

which results in further arterial stiffness (Taquet *et al.*, 1993). In addition, PWV was directly associated with biological variables such as heart rate, age, total cholesterol, LDL, triglycerides, apolipoprotein B, fasting glucose and BMI but not with HDL, apolipoprotein A1 and fibrinogen (Taquet *et al.*, 1993).

2.4.3 Methods of Measuring PWV

Pulse wave velocity testing is performed by measuring the speed of the blood pressure wave as it travels between two sets of anatomical points within the arterial system (Miyatani *et al.*, 2009). A transcutaneous Doppler probe is placed at each site and the pulse waveforms are recorded. The time delay between the beginning of the systolic upstroke at each site is measured. The PWV is calculated as the distance travelled divided by the measured wave latency between the two arterial recording sites and it is usually expressed in cm/s (Miyatani *et al.*, 2009). Aortic PWV values greater than 1300cm/s have been directly linked with cardiovascular mortality, fatal and non-fatal coronary events, and fatal strokes in patients with either low or high levels of traditional CAD risk factors (Miyatani *et al.*, 2009).

2.4.4 Methods of Assessing PWV

There are two sites of measurement used for PWV. The first is 'global' or 'central' PWV which measures long arterial trajectories and is most commonly measured between the carotid and femoral artery (Hermeling *et al.*, 2007). This global measure best describes the PWV along the aorta. The aorta is a major vessel of interest for many reasons. First, the aorta evolves from a large, elastic artery in the thoracic area to a more muscular vessel within the abdomen and iliac bifurcation and therefore cannot be categorized as either elastic or muscular but likely reflects a mix of properties related to

both (Vermeersch *et al.*, 2008). In addition, the thoracic and abdominal aortas are the largest contributors to arterial buffering function and aortic PWV is an independent predictor of outcome in many populations (Laurent *et al.*, 2006). One disadvantage of measuring central PWV is that the carotid and femoral pulse waves travel in opposite directions. This causes a chance of error in distance measurement as they are done topically. As such, the distance from the carotid artery to the femoral artery may be underestimated. Therefore, the use of the topical distance between carotid and femoral artery may cause an overestimation of the PWV (Hermeling *et al.*, 2007), however, so long as a consistent measure is used, this technique may be ideal for detecting changes in central PWV before and after an intervention.

The second method is known as ‘local’ or ‘peripheral’ PWV. In this method, the blood pressure wave is measured along a small arterial trajectory, such as the brachial artery to the radial artery or the femoral artery to the posterior tibial artery (Hermeling *et al.*, 2007). Although global PWV, or PWV measured along the aortic and aortoiliac pathways, is more clinically relevant as the aorta and its first branches are responsible for most of the pathophysiological effects of arterial compliance (Boutouyrie *et al.*, 2002), it is important to measure peripheral PWV as well. The measurement of peripheral PWV determines whether localized exercise using the upper and lower limbs affects arterial compliance in these limbs. For example, whole-body vibration may have the effect of increasing arterial compliance in the vessels of the lower limbs. This is important for individuals living with a SCI, as it may potentially help to decrease the risk of a DVT formation.

2.4.5 PWV and Individuals with SCI

PWV has been shown to be a useful and effective non-invasive measure to evaluate arterial compliance and severity of CVD among able-bodied people (Boutouyrie *et al.*, 2002; Taquet *et al.*, 1993). Few studies known to date have investigated the use of PWV with individuals with SCI. Miyatani and colleagues (2009) compared a cohort of 12 individuals with SCI to age, gender, height and weight matched able-bodied controls. Participants from both the SCI and control groups were excluded if they had a history of CVD or current metabolic syndrome. This study found that mean aortic PWV was significantly greater in the SCI group than the control group ($1274 \pm 369\text{cm/s}$ to $948 \pm 110\text{cm/s}$, $p < 0.05$). However, no significant differences were seen when arm and leg PWV values were compared. This was thought to be due to the fact that aortic PWV is sensitive to the level of daily activity and aging whereas arm or leg PWV is not. Also, because the central arteries have the function of dampening the central fluctuations in flow they may undergo more adaptations leading to a loss of elasticity than the peripheral arteries. This is in contrast to the study by Jae and colleagues (2008) that noted a decrease in compliance in the femoral artery in people with SCI as measured by augmentation index. The disparity in these findings warrants further study of the effects of SCI on arterial compliance. Mechanisms that may potentially account for the higher aortic PWV among individuals with SCI are the structural changes in the vessel as a result of long-term sympathetic dysfunction, increased collagen content in the vascular wall and functional changes in the endothelium caused by a decrease in regional blood flow (Miyatani *et al.*, 2009). The experiment performed by Miyatani and colleagues (2009) compared individuals with SCI and able-bodied individuals who did not have a history of CVD or metabolic syndrome. These results, which demonstrate a higher PWV among the SCI

population, may indicate reduced arterial compliance predisposing them to increased risk of cardiovascular events.

2.4.6 Inter- and Intra-Observer Reliability of PWV

Pulse wave velocity has been shown to be a valid and reliable estimate of arterial stiffness in able-bodied individuals. A study conducted by Lehmann *et al.* (1992) determined the coefficient of variation (CV) of intra- and inter- observer repeatability of aortic PWV in healthy individuals. The results showed a CV of 8.5% intra-observer and 9.4% inter-observer repeatability (Lehmann *et al.*, 1992). In addition, studies by Lee *et al.* (2009) and Naidu *et al.* (2005) used correlations to examine intra- and inter-observer reliability for various PWV measurements along the arterial tree. In 17 healthy subjects, intra-observer test-retest values for aortic, arm and leg PWV were highly repeatable within each vessel with r -values between 0.94 and 0.99 ($p < 0.01$). Inter-observer test-retest values for aortic, arm and leg PWV showed a more variable degree of repeatability among vessels, with r -values of 0.93, 0.50 and 0.58, respectively ($p < 0.05$) (Lee, 2009). Similarly, in the study by Naidu *et al.* (2005), heart-brachial, heart-ankle, brachial-ankle, and carotid-femoral PWV were tested in 44 healthy individuals in addition to individuals with CVD. Intra- and inter-observer correlations were found to be significant ($p < 0.0001$) with r values greater than 0.71 (Naidu *et al.*, 2005). However, one study found a significant intra-observer difference for aortic PWV despite no significant inter-observer difference. There was also no difference found for intra- or inter-observer brachial PWV (Frimodt-Moller *et al.*, 2008). Therefore, despite the demonstrated repeatability of PWV, it may still be necessary to conduct inter- and intra-observer repeatability calculations to ensure proper interpretation of results. As they have never been evaluated after SCI,

future studies should determine the inter- and intra-observer reliability for PWV in this population.

2.5 Benefits of Exercise for Individuals with a SCI

2.5.1 Arterial Compliance and Exercise

The effect of exercise on arterial compliance has been studied in the able-bodied population. The Baltimore Longitudinal Study on Aging showed that older endurance-exercise trained males demonstrated a lower aortic PWV and carotid augmentation index than their sedentary male peers (Vaitkevicius *et al.*, 1993). In a study by Boreham *et al.* (2004), males and females participated in an evaluation of their VO_{2max} as well as a PWV measurement of the central and peripheral vessels. Participants also answered a questionnaire about their exercise and sport participation. The central and peripheral PWV's were significantly and inversely related to VO_{2max} and participation in sport exercise was significantly and inversely related to the peripheral PWV but not the central PWV. It was thought that sport had a greater effect on the periphery with increased blood flow through the limbs causing the release of nitric oxide from the endothelium as well as some structural remodeling of the vessels (Boreham *et al.*, 2004). Age- related decreases in arterial compliance have been shown to be attenuated by aerobic exercise training (Tanaka *et al.*, 2000). With the increased arterial compliance due to aerobic training, the time to exhaustion increased by 20% and the heart rate and ratings of perceived exertion at the same absolute submaximal level of exercise decreased (Tanaka *et al.*, 2000). Heffernan *et al.* (2007) measured aortic PWV 20 minutes after an acute bout of endurance (30 minutes, 65% VO_{2max}) or strength training (3 sets of 10 repetitions at 100% of 10-repetition maximum) exercise in recreationally active men. The results

showed that arterial compliance was increased following the acute endurance exercise, while after the acute resistance exercise, arterial compliance was decreased. The acute changes due to aerobic exercise were thought to be due to intrinsic changes in arterial wall properties and not changes in vascular pressure as the changes were independent of mean arterial pressure. Otsuki *et al.* (2007) measured arterial compliance in endurance and strength trained athletes who had been training for over 2 years (long-term effects), 5 times per week at 3 hours per week. To account for the differences in arterial compliance after strength and endurance training, these authors also measured plasma endothelium-1 levels and plasma nitric oxide. The results showed that plasma nitric oxide did not differ but plasma endothelium-1 levels were greater in magnitude by 20% after strength training and thus may play a role in the different adaptations of arterial compliance following endurance and strength training protocols. Another study performed by Maeda, *et al.*, (2008) evaluated arterial compliance in older women after an acute bout of endurance exercise before and after an endurance training protocol. Interestingly, the acute exercise did not cause an increase in arterial compliance before training but did cause a significant increase following the exercise training protocol.

In contrast to aerobic training, resistance training increases proximal aortic stiffness and is associated with higher incidence of left ventricular hypertrophy compared to sedentary controls (Zieman *et al.*, 2005). Lastly, it has been found that stiffer vessels at rest experience higher pulse pressure at maximal exercise. This pressure, in turn, may limit cardiac output by increasing the energetic cost for the heart to maintain adequate blood flow (Kingwell, 2002). Therefore, it follows that when a population is susceptible to arterial events due to a decrease in arterial compliance, there may be value in

implementing an aerobic exercise program that may increase arterial compliance and reduce the associated cardiovascular risk. Therefore, these studies establish a link between aerobic exercise and arterial compliance, and the well-documented association of aerobic exercise benefits to cardiopulmonary fitness.

2.5.2 Challenges of Exercise for Individuals with SCI

Exercise is a main component and important aspect of what is considered to be a healthy lifestyle. The many benefits of exercise for the able-bodied population have been very clearly described within the literature (Hopp, 1993; Mayo & Kravitz, 1999; Morris & Froelicher, 1993). For individuals with SCI, the benefits from exercise are at least as important. This is due to the secondary health complications and associated morbidity and mortality attributed to the sedentary lifestyle that commonly follows the injury. The SCI population falls within the low end of the physical activity spectrum (Elder *et al.*, 2004). High-level thoracic and cervical injuries cause the greatest loss in muscle mass affecting prime movers and stabilizers of the trunk making exercise more difficult to complete. The cardiovascular power of an individual living with a SCI is substantially lower than the able-bodied population. The average VO_{2max} for individuals living with tetraplegia was found to be only 12mL/kg/min (de Groot *et al.*, 2006). Unfortunately, exercise within this population is more difficult than for the able-bodied population, and exercise options are severely limited. As mentioned, autonomic disruption, due to the lesion in the spinal cord, causes physiological responses to exercise to differ in the SCI population in comparison to the able-bodied population (Nash, 2005). Following an injury above T6, substantial adrenergic dysfunction occurs, decreasing regulatory input and altering the cardiovascular efficiencies achieved by able-bodied exercisers (Nash,

2005). In the able-bodied population, the sympathetic nervous system vasoconstrictor responses serve to increase the venous return and improve the end diastolic ventricular volume while heart rate and myocardial contractility increase. With high level and complete SCI, there is reduced sympathetic efferent output with lack of vasoconstriction and a reduced contractility response, however, there is some increased heart rate response as a result of reduced vagal withdrawal (Teasell *et al.*, 2000).

Not only is it more physically difficult for individuals with SCI to exercise, it has been shown that exercise adherence is also a problem in this population. In a study conducted by Anderson in 2004, 681 individuals living with a SCI were surveyed regarding the importance of exercise in their rehabilitation programs. Of these participants, 96.5% believed exercise was important and vital to their functional recovery, but only 57% had access to suitable exercise equipment and only 45% of this sub-group had access to a trained therapist (Anderson, 2004). To stress the importance of exercise adherence, Ditor *et al.*, (2003) measured pain, stress and perceived quality of life 3 months following a 9 month training protocol. During the 9 months of exercise training, pain and stress decreased by approximately 10% and perceived quality of life increased over 15%. In the 3-month follow up, exercise adherence decreased compared to during the 9-month program (42.7 versus 80.6%, respectively) and as a result pain and stress increased by 30% and 35% respectively. As well, there was a 10% decrease in perceived quality of life (Ditor *et al.*, 2003). Therefore, although exercise is necessary in order to maintain exercise-related increases in psychological well-being, adherence to exercise has shown to be a notable obstacle after SCI.

Aerobic exercise studies have been shown to raise arterial compliance in the able-bodied population (Tanaka *et al.*, 2000; Thijssen *et al.*, 2007). Likewise, aerobic exercise may also be beneficial for the SCI population and early studies have confirmed such a benefit. For example, Jae *et al.*, (2008) compared individuals living with paraplegia who regularly participated in aerobic exercise to recreationally active, age-matched, able-bodied controls. The results showed that regular exercise for individuals living with SCI eliminated any differences in mean carotid intima media thickness when compared to able-bodied controls. Therefore, aerobic exercise may help to preserve arterial function in individuals living with SCI (Jae *et al.*, 2008).

2.5.3 Modalities and Cardiovascular Benefits of Exercise

Common modalities of exercise, which significantly affect cardiovascular outcomes for individuals with SCI, include arm ergometry, body-weight supported treadmill training (BWSTT) and functional electrical stimulation (FES). Arm ergometry is most commonly used for endurance training and improvements in aerobic capacity. Studies have shown that arm ergometry can improve physical conditioning by an average of 15-25% (Cowell *et al.*, 1986; Davis *et al.*, 1981; Franklin, 1985). However, this modality is limited to those with fully or highly functioning upper limbs, as individuals living with low level tetraplegia who performed this exercise had their gains in peak oxygen uptake fail to approach those of individuals with lower level injuries (Yim *et al.*, 1993). Therefore, the more disabled individuals within the SCI population may not benefit from this form of exercise.

Ditor and colleagues (2005) used BWSTT for individuals with motor-complete injuries and investigated the effects on vessel cross-sectional area, blood flow, vessel

resistance and arterial compliance. Following four months of BWSTT, there was no significant exercise induced change in femoral and carotid cross-sectional area, blood flow or resistance. However, femoral arterial compliance significantly increased by approximately 50%. As well, Phillips and colleagues (2004) found that BWSTT decreased the risk for type-2 diabetes by decreasing resting plasma glucose levels and increasing GLUT-4 content, glycogen, ATP and PCr, ultimately leading to an improved glycemic regulation. By reducing the risk of type-2 diabetes, the risk for subsequent changes in the arterial endothelium are reduced and may have an effect on reducing arterial stiffness. A drawback of BWSTT is that it is a very expensive and labour intensive form of exercise. The average individual living with a SCI will be unable to perform this type of exercise at their own home. Therefore, it is necessary to identify a form of exercise that is less expensive and can be performed with minimal assistance to allow for individuals living with SCI to exercise at home.

Lastly, FES has shown promise as a cardiovascular stimulus. Enhanced levels of fitness have been shown following FES exercise (Mutton *et al.*, 1997) and it has been shown to reverse the adaptive left ventricular atrophy reported in individuals living with tetraplegia by significantly improving lower extremity circulation following training (Gerrits *et al.*, 2001). Thus, FES has a positive effect on reducing the risk of CVD in individuals living with tetraplegia. However, there are risk factors to this form of exercise including pain in those with spared sensation, and lack of response in those with lower motor neuron injuries.

2.6 Whole-Body Vibration (WBV)

2.6.1 What is WBV?

Whole-body vibration (WBV) is a relatively new form of exercise that has been explored as a means to benefit the musculoskeletal system as well as the cardiovascular system, and it typically entails individuals performing dynamic or static exercises, such as a squat, while standing on a vibrating platform. During this form of exercise, the vibrations emanating from the platform cause the human body to oscillate, thus causing a reactive force within the body (Rittweger, 2010). The platform oscillates vertically or in a sinusoidal direction at a specific frequency and amplitude. The frequency (Hz) represents the rate at which the platform vibrates and the amplitude (mm) represents the vertical displacement of the platform. Typically, frequency ranges between 26 to 45Hz and the amplitude ranges between 1-6mm. The human body is not rigid and has muscles and tendons that can store and release mechanical energy. In WBV, compression occurs during the vibration upstroke, and the opposite expansion occurs during the downstroke (Rittweger, 2010). The compression forces are believed to cause an increase in shear force along the vessel walls which is thought to cause deformation of the vessel. Deformation of a vessel stimulates the endothelial cells to release nitric oxide (NO) and promote vasodilatation (Chen *et al.*, 2002). Moreover, as the vibrations are transmitted through the body, they elicit a stretch reflex in the muscles. The vibrations cause the stretch of muscle fibres and the sensory organs within the muscles known as the muscle spindles. The muscle spindle sends a positive excitation signal to the alpha motor neuron of the muscle and causes a muscle contraction (Rittweger, 2010). This neuromuscular response is known as the 'tonic vibration reflex'. This reflex is thought to have the potential to increase the recruitment of motor units (Seidel, 1988). While an individual is performing a squat or other dynamic exercise, the positive stimulus of the vibration is

summated with the volitional positive excitation of muscle activation and results in the firing of more motor units with an augmented muscle force of contraction. This has the potential to produce an increase in strength development during an exercise program (Rittweger, 2010).

The waves of vibration are transmitted from the feet throughout the muscles of the body. As the vibration travels more proximally from the feet, the strength of the vibration is reduced (Rees *et al.*, 2008). In addition, the angle of knee and hip flexion are determining factors as to how high the vibration travels within the body. While standing fully erect, or nearly erect, with knees locked in extension, the vibration is transferred to the upper body, which may cause discomfort due to the shaking of the head and eyes (Rees *et al.*, 2008). Therefore, with individuals being placed in a squatting position where the weight is posed on the forefoot, the resonance of the vibration is dissipated in the abdomen thus minimizing the discomfort individuals experience (Rittweger, 2010).

2.6.2 Benefits of Long-term WBV Training

Assessment of the long-term training effects of WBV have mainly focused on muscular strength (Mester *et al.*, 2006; Roelants *et al.*, 2004) and have shown that vibrations induced increases of 5 to 35%. For example, a one year study of WBV training was conducted on adults over the age of 60 (Bogaerts *et al.*, 2009). This study had the participants dynamically exercising on the vibration platform. It was found that VO_2 peak increased by 18% following the vibration training and there was a 9.4% increase in muscular strength. In addition, heart rate increased to 62% of the heart rate reserve during the exercise signifying that WBV was effective in providing a cardiovascular stimulus in this population. A study evaluating the benefits of a 12-week, 5 times weekly, WBV

protocol at 30Hz for 5 minutes each day was done on individuals living with paraplegia who regularly participated in sport (Melchiorri *et al.*, 2007). It was found that the average muscle force, velocity and power were increased in the upper limbs following the 12-week protocol whereas body composition and bone mineral density did not change.

2.6.3 Benefits of an Acute Bout of WBV

The mechanical stimulation induced by the vibration on the platform has been shown to have positive acute effects. Whole-body vibration has been used on the able-bodied population to test the effects on cardiovascular outcomes. For example, Rittweger and colleagues (2001) have shown that vibration groups have a greater VO_2 peak than none-vibration controls. Conversely, another study found that VO_2 only increased when a Jendrassik maneuver (participant pulled with both arms on a dual-handle load cell) was performed in concert with the vibration. This is due to the summation of the stretch reflex excitation caused by the WBV and the excitation already placed on alpha motor neurons due to the Jendrassik maneuver. As such, it was concluded that WBV alone may not be a sufficient stimulus to elicit changes in cardiovascular fitness (Cochrane *et al.*, 2008). Yamada and colleagues (2005) found that WBV reduces muscle oxygenation levels compared to those without WBV. The contracting of the muscles, caused by the vibration, placed demands on the circulatory system for increased blood flow and therefore, it was concluded that WBV may be an efficient training stimulus. Mester *et al.* (2006) found that total peripheral resistance (TPR) and mean arterial pressure increased significantly during vibration with no change in cardiac output. To account for this increase in TPR, it was postulated that the vibration caused vessel deformation. Immediately after vibration, TPR dropped 25% below baseline levels and mean blood

pressure dropped 29% below baseline values. These adaptations were attributed to the opening of more capillaries or the dilation of some blood vessels in order to facilitate efficient gas and material metabolism between blood vessels and muscle fibres.

In the able-bodied population, one study has investigated the direct effect of WBV on arterial compliance using PWV as the experimental measure. Otsuki and colleagues (2008) assessed arterial compliance measuring brachial-ankle PWV in 10 healthy men pre-WBV as well as 20, 40 and 60 minutes after an acute bout of WBV. The protocol included a set vibration frequency of 26Hz, with intermittent vibration (60s on and 60s off) with the participants positioned in a static squat. The results showed that in the WBV group, the brachial-ankle PWV value significantly decreased denoting an increase in arterial compliance, at 20 and 40 minutes after the trial without any significant decrease in blood pressure. Also important to note, as previously mentioned, individuals with SCI have a risk for postural hypotension. The results from Otsuki and colleagues (2008) showed no reduction in blood pressure during WBV and therefore, this form of exercise was not associated with an increased risk for postural hypotension within this population. The mechanisms underlying the acute exercise-induced increase of arterial compliance may be related to the mechanical stimuli of the vibration causing a deformation of the endothelial cells, resulting in the release of NO and vasodilatation (Otsuki *et al.*, 2008).

Chapter 3: Inter- and Intra-Observer Reliability for PWV in Individuals with SCI

3.1 Methods of Assessing PWV Inter- and Intra-Observer Reliability in Individuals with SCI

The participants recruited for this reliability study, were recruited from the Lyndhurst Centre in Toronto, Ontario, and were the same participants that were involved in the acute WBV study described in Chapter 4 of this thesis. For inclusion into the study, participants had to be: male, between the ages of 20-60 years of age at the commencement of baseline measures, living with long-term SCI (C1 to T12, AIS A to E; over 1 year post-injury), having sustained the injury by traumatic etiology (motor vehicle accident, fall, sports injury, violence, etc). Refer to Appendix C for the Standard Neurological Classification of Spinal Cord Injury.

Participants were required to abstain from caffeine, nicotine and alcohol for 12 hours and to fast for a minimum of 6 hours prior to testing. For medications that were required to be taken with food, the participants were permitted water and up to one slice of bread. Participants were also asked to not partake in vigorous exercise for the 12 hours preceding the measurements.

Two identical Smartdop50 transcutaneous Doppler flowmeters (Hadeco, Inc., Kanagawa, Japan) were used and placed at the vascular landmarks on each participant to obtain a pair of measurements. The PWV measurement was taken at the aortic pathway. Transcutaneous flow waves were recorded with the use of Doppler flowmeters, and beat-by-beat data were visualized and recorded via Chart 5.2 software and a PowerLab/16SP data acquisition system (ADInstruments, Inc. Bella Vista, Australia).

The distance traveled by the pulse waveform was assessed by the measurement of the distance between two vascular landmarks over the surface of the body using a non-

elastic tape measure. Measurements of PWV were taken along the aorta (common carotid at the neck to the common femoral artery at the inguinal crease in thigh). The measurements were taken following 20 minutes of supine rest. PWV was calculated from this distance divided by the average of at least 20 wave latencies in cm/sec. Transit time was determined from the time delay between the proximal foot and the distal foot of the waveform (Figure 1). It is important to note that only the reliability of the data analysis was being conducted in this study, rather than the reliability of the PWV test (which would entail data collection and analysis). Thus, PWV measures were only conducted once, but analyzed twice, and the reliability of the analysis only was subsequently evaluated.

The data chosen for analysis was baseline aortic PWV values, and an intraclass correlation test was performed to determine whether a significant relationship existed between and within the testers. In addition, a Bland-Altman plot was used to determine if the magnitude of the baseline PWV had any bearing on its degree of reliability (Bland & Altman, 1986). Significance was set at $p \leq 0.05$, and all values are expressed as means \pm standard deviation (SD).

3.2 Results of Inter- and Intra-Observer Reliability Testing for PWV in Individuals with SCI

A total of eight participants were included in the study. All participants were male with an average age of 41.8 ± 10.7 years, a post-injury period of 11.0 ± 8.4 years, a weight of 79.9 ± 19.6 kg and height of 174.3 ± 6.3 cm. Based on the initial neurological examination provided by the American Spinal Injury Association (ASIA), five

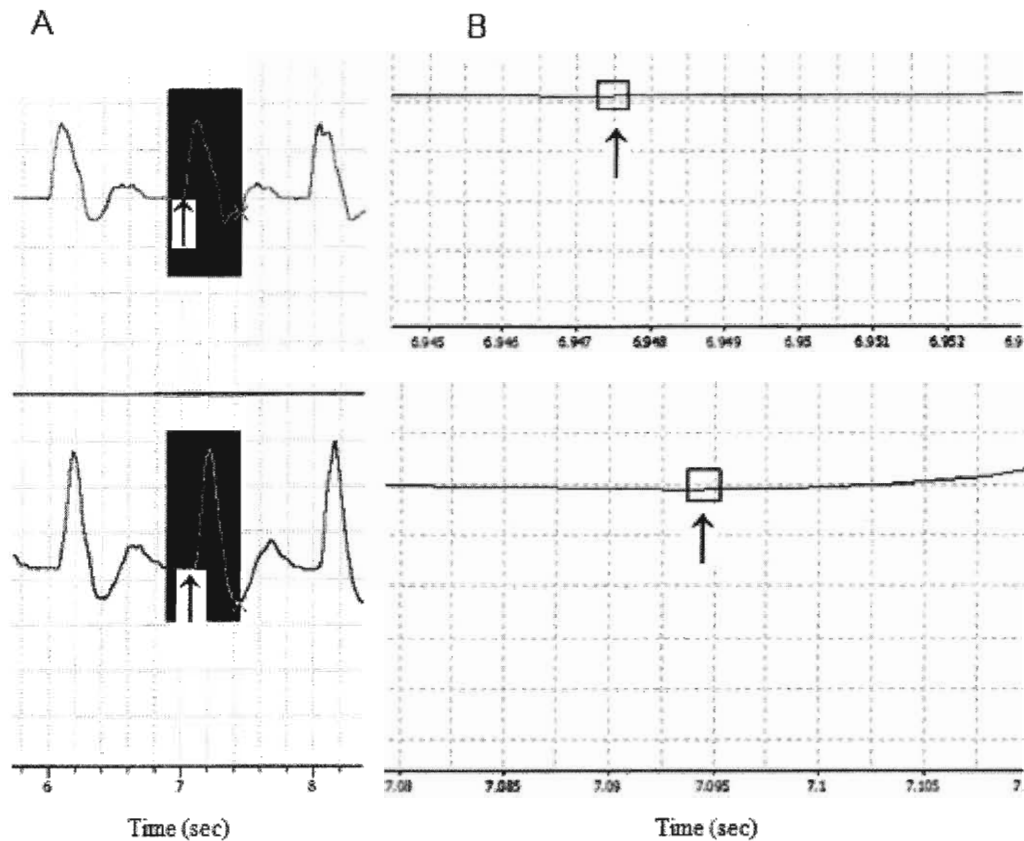


Figure 1: A) represents the blood pressure waves of aortic PWV, the red is the femoral artery and blue is posterior tibial artery. B) represents the zoomed view of the same highlighted blood pressure wave in A. The boxes represent the point on the wave when the systolic upstroke is beginning. The transit time is difference in time between these two points. Time (s) is on the X axis.

participants were classified as having a complete injury (ASIA Impairment Scale A; AIS A) and three as having an incomplete injury (AIS D). Lesions levels ranged from C4 to T11.

Observer 1 found an average baseline aortic PWV value of 946.0 ± 136.4 cm/s and Observer 2 found an average of 927.0 ± 172.2 cm/s (Table 1). The intraclass correlation analysis calculated the coefficient to be 0.76 ($p=0.006$). Figure 2 shows the Bland-Altman plot for this data. The points in this graph show no skewness, and therefore, the difference between observer analysis is not dependent on the mean.

Table 2 shows the intra-observer reliability. Analysis 1 calculated an average baseline aortic PWV value of 946.0 ± 136.4 cm/s while on analysis 2, an average baseline aortic PWV value of 954.0 ± 128.6 cm/s was calculated. The intraclass correlation coefficient was very high ($r=0.93$, $p<0.001$). Figure 3 shows the Bland-Altman plot for this data. The points in this graph show no skewness, and therefore, once again, the difference of intra-observer analysis is not dependent on the mean.

Table 1: PWV values (cm/s) for both observer 1 and observer 2.

Participant	PWV value for Observer 1 (cm/s)	PWV value for Observer 2 (cm/s)
1	875	848
2	851	825
3	1044	991
4	948	1201
5	815	771
6	902	811
7	894	803
8	1237	1169
Mean	946	927
SD	136.4	172.2

Table 2: PWV values (cm/s) for both analysis 1 and analysis 2 of observer 1.

Participant	PWV value for Analysis 1 (cm/s)	PWV value for Analysis 2 (cm/s)
1	875	822
2	851	833
3	1044	1082
4	948	997
5	815	889
6	902	948
7	894	871
8	1237	1187
Mean	946	954
SD	136.4	128.6

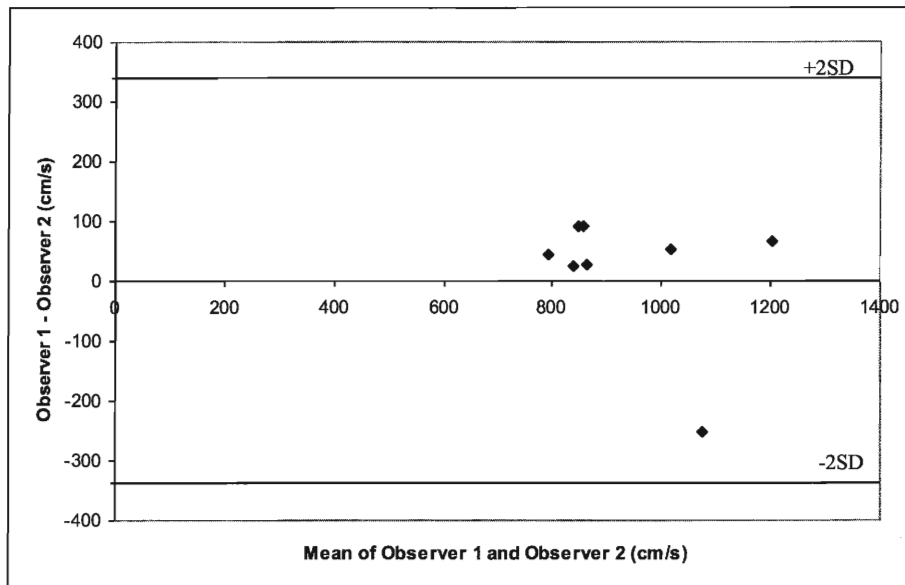


Figure 2: Bland-Altman plot for the inter-observer reliability for aortic PWV values showing observer 1 – observer 2 plotted against the mean of observer 1 and observer 2 values (cm/s).

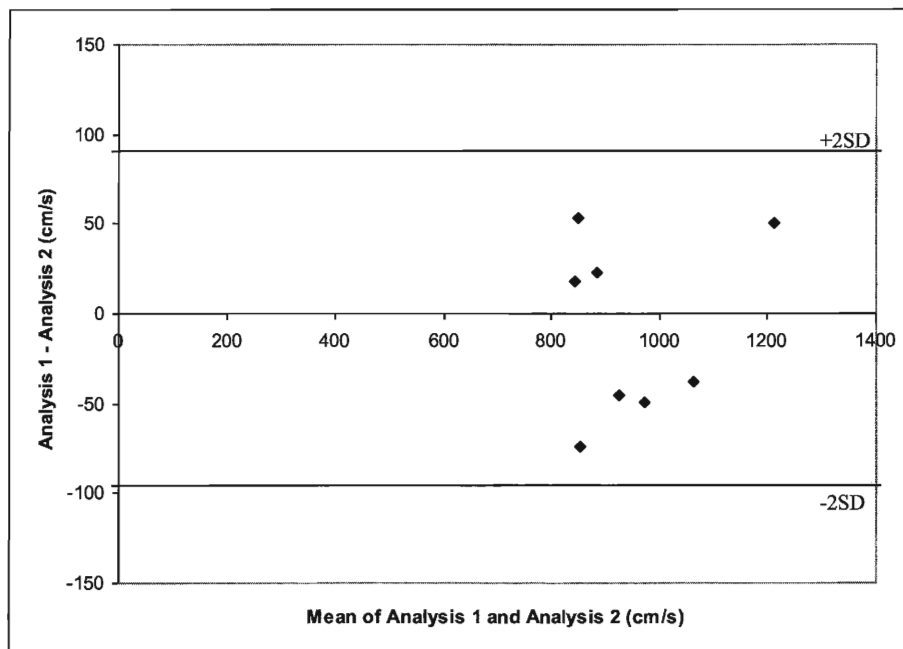


Figure 3: Bland-Altman plot for the intra-observer reliability for aortic PWV values showing analysis 1 – analysis 2 plotted against the mean of analysis 1 and analysis 2 values (cm/s).

Chapter 4 – The Effect(s) of Whole Body Vibration on Pulse Wave Velocity in Individuals with SCI

4.1 Methods

4.1.1 Participant Information

4.1.1.1 Participant Recruitment

The participants for the current study were recruited through the Lyndhurst Centre in Toronto, Ontario, Canada. The methods of recruitment included poster campaigns, referral by a rehab service provider, at the individual's request, or with the use of the SCI Long-term Follow-up database which contains a list of individuals interested in finding out more information about ongoing SCI research at the Lyndhurst Centre.

4.1.1.2 Participant Screening

Potential participants were asked to complete a telephone pre-screening interview to ensure that they did not have a prior history inconsistent with safe WBV. The telephone screening consisted of obtaining verbal consent to collect health and demographic information about the participant in order to determine the first stage of eligibility. This information included age, weight, height, traumatic/non-traumatic SCI, medical history and concomitant medications. Following the completion of a successful pre-screening process, a Letter of Introduction and Consent Form was mailed to each participant. These forms were reviewed by the participant prior to the screening visit. It was during this subsequent screening visit that written informed consent from the participant was obtained prior to conducting any study-related testing or evaluation. The screening visit began with the collection of written, informed consent in order to allow participation in the study. Any changes to the potential participant's medical history or medications since pre-screening were recorded. Once these were completed, a physical

examination, medical history, a blood test screening for anemia and vitamin D deficiency, an ultrasound of the kidney and bladder to rule out stones, and an X-ray of the spine for the assessment of hardware were completed by a trained physician.

4.1.1.3 Participant Inclusion and Exclusion Criteria

Prior to data collection, potential participants were required to meet inclusion and exclusion criteria. This information was gathered through the telephone interview and was reviewed and verified with their medical records and medical history during the screening visit.

The inclusion criteria for this study included: male participants between the ages of 20-60 years of age at the commencement of baseline measures; individuals living with long-term SCI (C1 to T12, AIS A to E; over 1 year post-injury) who sustained the injury by traumatic etiology (motor vehicle accident, fall, sports injury, violence, etc). Refer to Appendix C for the Standard Neurological Classification of Spinal Cord Injury.

The exclusion criterion included individuals with a height of less than 168cm or greater than 188cm. This height restriction was in place for safety as the vibration platform is only able to accommodate individuals within this specific range. Individuals with a history of uncontrolled autonomic dysreflexia, untreated orthostatic hypotension, seizure disorder, frequent migraine headaches, rheumatoid arthritis, current kidney stones, arrhythmias, valvular heart disease, non-union fragility fracture, dislocated hip, cochlear implants, DVT, spondylolisthesis, diabetes, gallstones, pacemaker, cancer or lower extremity pressure ulcer were excluded as these conditions may cause WBV exposure to be unsafe. In addition, participants with conditions which might make it difficult to stand safely in the standing frame such as combined hip and knee flexion

contractures of $>30^\circ$, plantar flexion contractures of $>20^\circ$, or bilateral heterotrophic ossification of the hip or knee region were excluded. Individuals were also excluded if they were concurrently participating in another intervention study or program that might confound interpretation of the study results. As well, individuals were excluded if they were unable to pass the postural retraining protocol, had anemia or vitamin D deficiency or the presence of kidney or bladder stones within 6 months of enrolment.

4.1.1.4 Postural Retraining Protocol

Following the screening visit, the participants were asked to perform a postural retraining protocol (PRP) prior to the WBV protocol (Appendix A). Each participant was required to complete the training within five sessions or they were excluded. Postural retraining employs a tilt to the individual on a tilt table, and if successful, helps the individual to better accommodate to changes in vertical position (as in going from sitting to standing) without undue hypotension or syncope. The PRP was deemed complete once the participant was able to tolerate going from a seated position to a near erect posture (85° tilt) and remain in the near erect posture for 30 minutes without symptoms of orthostatic hypotension. Figure (4) shows a timeline of the recruitment process.

4.1.1.5 Participants of the Current Study

A total of eight ($n=8$) participants were included in the study. All participants were male with an average age of 41.8 ± 10.7 years, a post-injury period of 11.0 ± 8.4 years, a weight of 79.9 ± 19.6 kg and height of 174.3 ± 6.3 cm. Based on the initial neurological examination provided by the American Spinal Injury Association (ASIA), five participants were classified as having a complete injury (ASIA Impairment Scale A; AIS A) and three as having an incomplete injury (AIS D). Lesions levels ranged from C4 to

T11. See Table 1 for participant characteristics. It is also important to note that during this study, no adverse events including orthostatic intolerance, autonomic dysreflexia or pressure sore development were observed.

Table 3: Participant Characteristics.

Participant	Level of Injury	ASIA Level	Age (years)	Time Post Injury (years)	Height (cm)	Weight (kg)
1	C4	D	36	13.2	173.0	73.2
2	T11	D	44	25.6	178.0	72.7
3	T10	A	53	8.6	173.5	82.3
4	T6	A	34	6.8	176.0	58.2
5	T6	A	42	20.9	169.0	105
6	T8	D	43	1.1	187.4	109.1
7	T4	A	24	7.5	168.0	55.0
8	T3	A	58	4.4	169.5	84.1

4.1.2 Acute Whole-Body Vibration Protocol

4.1.2.1 Experimental Timeline

The purpose of this study was to determine the acute effect(s) of WBV on arterial compliance. A change in PWV was used to indicate a change in arterial compliance. After initial screening and the PRP, a passive stance (PS) protocol was performed. The PS protocol acted as a control for the possible changes in PWV resulting from assuming the upright position. The WBV protocol was implemented approximately 1 week following the completion of the PS protocol. Refer to Figure 4 for timeline of the screening and training protocols.

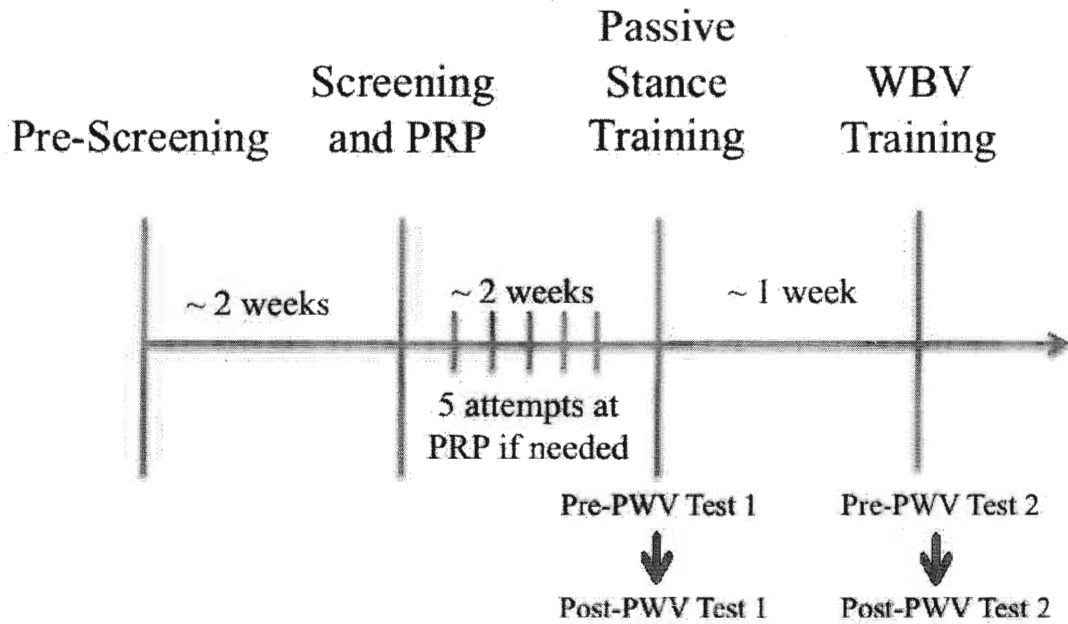


Figure 4: Timeline of Participant Recruitment and Protocol

4.1.2.2 Passive Stance Protocol

The purpose of the PS test was to control for the possible effects of the upright position when testing for the effects of WBV on arterial compliance. All of the PS sessions were performed at the Lyndhurst Centre. On this day, the participants entered the lab, transferred onto a bed and rested for 20 minutes in a supine position. Supine PWV measurements of the arm (brachial to radial artery), aorta (common carotid to femoral artery) and leg (femoral to posterior tibial artery) were taken in a random order. These measurements acted as the baseline values to compare to the values following the passive stance protocol. During the PS protocol, participants were elevated to a near complete upright position with knee flexion of 160° (full knee extension = 180°). The elevation to the upright position was controlled by the participant using the Easy Stand 5000 (Easystand, Minnesota, USA), and took approximately 1-2 minutes, to avoid a dramatic decline in blood pressure. The participants' thighs and calves were supported by cushions to maintain knee flexion and extra support for balance was allowed by leaning

on a shelf at the front of the apparatus. Prior to beginning passive stance, the participants were asked to void their bladder and bowels. In addition, an abdominal binder was placed on the participant prior to elevation to help prevent orthostatic hypotension and extra gel cushions were placed at the knees and lumbar spine to prevent pressure sore formation. The participants remained in this PS position for a total of 45 minutes. At 30 minutes, the participants were lowered back to a sitting position to check pressure areas such as the knee and lumbar spine, using the blanching technique, to detect any new skin irritations. If the circulation remained adequate to prevent such irritations, the participant was elevated back to the upright position to complete the final 15 minutes. Following the completion of the 45 minutes of passive stance, the participants were returned to the supine position. PWV measurements of the three sites were then completed at 10 minutes following the passive stance.

Blood pressure (BP), as measured by manual auscultation and heart rate (HR), as measured by a heart rate monitor (Polar, New York, USA) were carefully monitored throughout the entire protocol to ensure safety for the participant. Blood pressure and HR were first taken after the 20-minute rest period to ensure no adverse events prior to commencing any testing. Blood pressure and HR were measured again in the seated and upright positions to ensure that there were no signs of orthostatic hypotension, and then again at 15-minute intervals during the passive stance protocol. Lastly, BP and HR were monitored again after 5 minutes in the supine position upon completion of the passive stance protocol. Blood pressure was converted to mean arterial pressure (MAP) for analysis. The equation used was $MAP = 2/3(\text{diastolic pressure}) + 1/3(\text{systolic pressure})$.

4.1.2.3 WBV Protocol

The WBV training protocol consisted of a 45-minute session one week following the passive stance protocol. All of the sessions were performed at the Lyndhurst Centre. The protocol of WBV is as described for the passive stance with the addition of the WBV while standing on the platform. Each participant was exposed to intermittent 45Hz vibration with a displacement of 0.6mm on a modified WAVE[®] platform (WAVE Manufacturing Inc, Ontario, Canada). Refer to Appendix E for visual representations of the apparatus. Each intermittent vibration cycle consisted of 60 seconds of vibration followed by 120 seconds of no vibration. These cycles alternated for a total of 15 minutes and 3 sets for a total of 45 minutes. At the end of each set, BP and HR were measured and after 30 minutes, the skin circulation at the knees was checked as in PS. In addition, to reduce the risk of autonomic dysreflexia during PS and WBV, the participants were asked to empty their bowel and bladder. As well, to prevent orthostatic hypotension, an abdominal binder was placed on the participant prior to both protocols. Participants were monitored for and were asked to report any signs and symptoms of autonomic dysreflexia and BP was monitored to detect potential episodes of autonomic dysreflexia.

4.1.3 Experimental Measures

4.1.3.1 Pulse Wave Velocity

Pulse wave velocity was chosen as the assessment tool for arterial compliance due to its association with cardiac events (Abhayaratna *et al.*, 2008) and its relationship with other cardiovascular risk factors (Taquet *et al.*, 1993). In addition, as stated in Chapter 3, PWV has high inter- and intra-observer reliability and therefore can be used with confidence for the assessment of arterial compliance. The PWV measurement technique

was identical to that described in Section 3.1 (p. 47-48). However, in this protocol, PWV measurements were taken at the arm (brachial artery at inner arm to radial artery at the wrist), leg (common femoral at inguinal crease to posterior tibial artery posterior to lateral malleolus) and aortic (common carotid at the neck to common femoral artery) pathways. These sites were included to determine the effect of WBV exercise on arterial compliance in the central and peripheral vasculature as measured by PWV.

4.1.4 Statistical Analysis

Descriptive statistics were used to describe the participant's baseline demographic and impairment characteristics. A 2-way (condition by time) repeated measures ANOVA was used to detect potential changes in PWV evoked by WBV compared to passive stance. In addition, a 1-way ANOVA was used to determine any significant differences between pre- and post- values for both PS and WBV trials. Other cofactors may account for any changes or lack of changes seen after WBV. Therefore, ten 2-way (condition by time) repeated measures ANCOVA calculations were performed per vessel measured to cofactor these variables. The variables included anthropometric measures (age, height, weight), injury characteristics (time post-injury), and cardiovascular measures (baseline PWV, baseline HR, change in HR from rest to WBV, baseline MAP, the change in MAP from rest to WBV and lastly, HR and MAP following WBV). Pearson r correlations were also performed on the same cofactors as the ANCOVA measurements to test possible relationships between these variables and potential changes in PWV after WBV.

SCI specific characteristics are thought to affect the response to exercise. Therefore, in addition to performing the PWV analysis on the participants as a whole, the participant pool was divided into groups based on the level and severity of injury. The

level of injury was categorized as a neurological level either above or below T5. This threshold was chosen as the heart is sympathetically innervated by fibres originating from T1 to T4 and therefore cardiac autonomic dysfunction is expected in injuries at and above this level. In addition, with injuries above T5, the splanchnic vascular bed which is innervated from T6-T12, is at least partially disconnected from the vasomotor centre in the brain and there is vascular autonomic dysfunction with exercise. Thus, with SCI above T5, there is a reduced cardiac response as well as reduced vasoconstriction via the splanchnic nerves and therefore, a decreased ability of the heart and vessels to respond to exercise.

For any given level of injury, a greater severity of injury is expected to worsen the ability of the heart and vessels to respond appropriately to exercise. In addition, WBV is thought to recruit muscle fibers for increased muscle contraction activity via the tonic vibration reflex (TVR). The TVR excitation of the motor neurons may summate with the other excitatory input on the motor neurons producing a larger and stronger muscle contraction. As such, the WBV may result in a stronger muscle activation response with lower level and incomplete SCI. With the increased muscle firing there is the potential for an increased cardiovascular conditioning effect. Thus, the effects of WBV on PWV were also determined separately for those with complete (AIS A) and incomplete (AIS D) SCI.

Therefore, participants were grouped based on level and severity of injury and a 2-way (condition by time) repeated ANOVA was used to detect potential changes in PWV evoked by WBV compared to passive stance within these groups. In addition, a 1-

way ANOVA was conducted to determine any baseline PWV differences between the groups.

Statistical significance was set at $p \leq 0.05$ and all values are expressed in means \pm standard deviation (SD). Effect sizes were also calculated to determine whether our sample size was sufficient to witness significant changes (Keppel & Zedeck, 1989).

4.1.5 Safety and Caution Considerations

4.1.5.1 Adverse Events

All individuals were closely monitored for the development of any adverse responses. In particular, the adverse events that were closely monitored were orthostatic hypotension, autonomic dysreflexia and the effects of pressure on the skin. The testing was to be stopped immediately upon any event that was deemed to jeopardize the health of the participant. This decision was left to a physician who would evaluate the situation and determine if the protocol could continue or not. The protocol was to be resumed if and when the same physician deemed it safe to do so.

4.1.5.2 Orthostatic Hypotension

For safety of each participant, blood pressure was measured at arrival, during quiet standing in the standing frame prior to vibration exposure, and at 15-minute intervals until the training session was complete. Changes in blood pressure between sitting, standing, and vibration were monitored, and if the participant showed signs of severe orthostatic hypotension between sitting and standing, the vibration was not commenced. If hypotension developed during the WBV, the WBV was stopped. Severe orthostatic hypotension was operationally defined as a drop in systolic blood pressure below 70mmHg, diastolic blood pressure below 40mmHg or heart rate below 50bpm.

4.1.5.3 Autonomic Dysreflexia

If a participant demonstrated signs of moderate autonomic dysreflexia, indicated by a rise of greater than 40mmHg in systolic blood pressure, the vibration session was to be stopped and the subject monitored until symptoms resolved. The subject was to be transferred to a monitored setting if the autonomic dysreflexia was severe or persisted. Signs and symptoms included sweating above the lesion, a flushed face, and a pounding headache in addition to the rise in blood pressure.

4.1.5.4 Pressure Sores

Pressure sores were monitored using the NPUAP grading scale (Appendix B). Because there was potential for participants to develop anterior knee-region pressure sores and pressure areas on the bony prominences of the sacrum and coccyx with the PS and WBV protocols, precautions were taken with the gel cushion. If a participant's skin was at risk during the PS or WBV as determined by the blanching technique, the testing was to be terminated.

4.2 Results

4.2.1 Pulse Wave Velocity

4.2.1.1 All Participants

Three separate 2-way repeated measures ANOVA's were used to determine whether there was a condition by time interaction when examining PWV in the aorta, leg and arm. There was no significant interaction found for either the aorta ($p=0.64$, Figure 5), leg ($p=0.80$, Figure 6) or arm PWV ($p=0.92$, Figure 7). A 1-way ANOVA was then performed to determine whether PS or WBV had a significant effect on PWV. In addition, effect sizes (ES) were calculated to determine whether our sample size was

sufficient to witness significant changes. Following PS, there was no significant change in PWV along the aorta (946.2 ± 136.6 vs. 936.3 ± 185.4 cm/s, $p=0.73$, $ES=0.11$) or the arm (1101.8 ± 154.8 vs. 1170.2 ± 197.5 cm/s, $p=0.21$, $ES=0.25$). However, leg PWV did show a significant 7.1% increase (1025.4 ± 76.1 vs. 1098.0 ± 94.7 cm/s, $p=0.05$, $ES=0.39$). One-way ANOVA showed no significant changes in PWV following WBV (aorta: 928.6 ± 127.7 vs. 901.1 ± 96.6 cm/s, $p=0.12$, $ES=0.12$; leg: 1035.2 ± 113.8 vs. 1099.8 ± 114.2 cm/s, $p=0.11$, $ES=0.27$; arm: 1118.9 ± 119.8 vs. 1181.1 ± 124.40 cm/s, $p=0.28$, $ES=0.25$).

4.2.1.2 Level of Injury

Three participants were classified with injuries above T5 and five participants below T5. In individuals with an injury above T5, there was no significant condition by time interaction for aortic PWV (pre-PS: 1002.0 ± 203.7 vs. post-PS 1048.3 ± 271.1 cm/s; pre-WBV: 1005.3 ± 180.6 vs. post-WBV: 934.7 ± 155.0 cm/s, respectively, $p=0.17$, Figure 8). There was also no significant condition by time interaction for aortic PWV in individuals with injuries below T5 (pre-PS: 912.0 ± 89.4 vs. post-PS: 869.2 ± 91.4 cm/s; pre-WBV: 881.4 ± 70.8 vs. post-WBV: 880.2 ± 53.9 cm/s, $p=0.14$, Figure 9).

In individuals with an injury above T5, there was no significant condition by time interaction for leg PWV (pre-PS: 1059.3 ± 70.9 vs. post-PS: 1110.3 ± 38.9 cm/s; pre-WBV: 972.3 ± 45.8 vs. post-WBV: 1088.3 ± 97.4 cm/s, $p=0.50$, Figure 10), however, for individuals with injuries below T5, there was a trend for a condition by time interaction for leg PWV following WBV compared to PS (pre-PS: 1004.0 ± 78.7 vs. post-PS: 1090.0 ± 121.5 cm/s; pre-WBV: 1072.8 ± 129.9 vs. post-WBV: 1104.6 ± 134.0 cm/s, $p=0.06$, Figure 12). That is, the increase observed in leg PWV was less after WBV than with PS.

In individuals with an injury above T5, there was no significant condition by time interaction for arm PWV following WBV compared to PS (pre-PS: 1109.7 ± 271.7 vs. post-PS: 1203.3 ± 336.7 cm/s; pre-WBV: 1057.0 ± 139.0 vs. post-WBV: 1152.3 ± 153.0 cm/s, $p=0.97$, Figure 11). In addition, there was no significant condition by time interaction for arm PWV in individuals with injuries below T5 (pre-PS: 1095.4 ± 70.2 vs. post-PS: 1149.4 ± 101.1 cm/s; pre-WBV: 1155.2 ± 104.6 vs. post-WBV: 1198.6 ± 119.9 cm/s, $p=0.91$, Figure 13).

Three 1-way ANOVA's were conducted to determine if any baseline differences existed between the groups before WBV. Aortic baseline PWV showed no significant differences (above T5: 1005.0 ± 180.6 cm/s; below T5: 881.0 ± 70.8 cm/s; ES=0.41; $p=0.74$; Figure 23) between the groups. However, trends were shown for leg (above T5: 972.0 ± 45.8 cm/s; below T5: 1073.0 ± 130.0 cm/s; ES=0.46; $p=0.07$; Figure 24) and arm (above T5: 1057.0 ± 139.6 cm/s; below T5: 1155.0 ± 104.6 cm/s; ES=0.37; $p=0.06$; Figure 25) baseline PWV. Thus, leg and arm baseline PWV tended to be higher in individuals with injuries below T5. The effect sizes showed a moderate effect, and therefore statistical significance may have been achieved with greater sample size.

4.2.1.3 Severity of Injury

Three participants were classified with incomplete injuries and five participants with complete injuries. In individuals with complete injuries, there was no significant condition by time interaction for aortic PWV (pre-PS: 987.6 ± 162.4 vs. post-PS: 980.2 ± 230.6 cm/s; pre-WBV: 940.8 ± 155.1 vs. post-WBV: 906.6 ± 123.7 cm/s, respectively, $p=0.70$, Figure 14). There was also no significant condition by time interaction for aortic PWV in individuals with incomplete injuries (pre-PS: 876.0 ± 25.5

vs. post-PS: 863.3 ± 33.5 cm/s; pre-WBV: 906.3 ± 88.6 vs. post-WBV: 890.7 ± 42.1 cm/s, $p=0.20$, Figure 15).

In individuals with complete injuries, there was no significant condition by time interaction for leg PWV (pre-PS: 1037.8 ± 79.6 vs. post-PS: 1064.4 ± 106.4 cm/s; pre-WBV: 1090.8 ± 95.2 vs. post-PWV: 1141.2 ± 120.7 cm/s, $p=0.67$, Figure 16). As well, in individuals with incomplete injuries there was no significant condition by time interaction for leg PWV following WBV compared to PS (pre-PS: 1003.0 ± 80.5 vs. post-PS: 1153.0 ± 35.0 cm/s; pre-WBV: 942.3 ± 81.1 vs. post-WBV: 1027.3 ± 66.0 cm/s, $p=0.20$, Figure 18).

In individuals with complete injuries, there was no significant condition by time interaction for arm PWV (pre-PS: 1165.8 ± 142.1 vs. post-PS: 1180.6 ± 238.9 cm/s; pre-WBV: 1179.2 ± 78.9 vs. post-WBV: 1205.0 ± 126.2 cm/s, $p=0.91$, Figure 17). In addition, there was also no significant condition by time interaction for arm PWV in individuals with incomplete injuries (pre-PS: 992.3 ± 123.6 vs. post-PS: 1151.3 ± 146.6 cm/s; pre-WBV: 1017.0 ± 114.6 vs. post-WBV: 1141.7 ± 136.3 cm/s, $p=0.21$, Figure 19).

Three 1-way ANOVA's were calculated to determine if any baseline differences existed between the groups before WBV. Neither aortic (complete: 941.0 ± 155.1 ; incomplete: 906.0 ± 88.6 cm/s; $ES=0.13$; $p=0.20$; Figure 26), leg (complete: 1091.0 ± 95.2 ; incomplete: 942.0 ± 81.1 cm/s; $ES=0.64$; $p=0.26$; Figure 27) nor arm (complete: 1179.0 ± 78.9 ; incomplete: 1017.0 ± 114.6 cm/s; $ES=0.64$; $p=0.29$; Figure 28) baseline PWV were significantly different between the groups. The effect sizes for the leg and arm are considered a large. Therefore, with more participants, a significant difference in

baseline PWV at the leg and arm may have been achieved when comparing those with complete and incomplete SCI.

4.2.1.4 Accounting for Other Cofactors

Ten potential cofactors were examined to see if the lack of significant changes in PWV following WBV were due to any confounding variables. These cofactors included anthropometric measures (age, height, weight), injury characteristics (time post-injury), and cardiovascular measures (baseline PWV, baseline HR, change in HR from rest to WBV, baseline MAP, the change in MAP from rest to WBV and lastly, HR and MAP following WBV). None of the variables tested were found to be significant cofactors as determined by 2-way repeated measures ANCOVA calculations. Refer to Tables 6-9 in Appendix D for ANCOVA tables and Figures 20-22 for the baseline PWV co-factor graphs.

4.2.1.5 Correlations

Pearson's r correlations were conducted to test whether the same cofactors used in the ANCOVA measurements correlated with the changes in PWV after WBV. A trend was found for time post-injury and the change in aortic PWV after WBV ($r=0.68$, $p=0.07$) such that, the more acute the injury, the greater the decrease in PWV after WBV. Refer to Table 10 and 11 in Appendix D for correlation coefficients and p values for all correlations.

4.2.2 Mean Arterial Pressure and Heart Rate

Table 5 in Appendix D shows the pre and post values for MAP and HR following PS and WBV. There was no condition by time interaction for either MAP or HR as

determined by 2-way repeated measures ANOVA. Further, a 1-way ANOVA showed no change in MAP following PS (99.1 ± 14.1 to 96.1 ± 6.8 , $p=0.46$) but a trend for an increase in HR (63.4 ± 7.8 to 66.8 ± 7.2 bpm, $p=0.07$). Similarly, a 1-way ANOVA showed no change in either MAP (98.3 ± 16.4 to 98.1 ± 14.9 , $p=0.35$) or HR (66.6 ± 7.9 to 64.1 ± 7.4 bpm, $p=0.23$) following WBV.

Chapter 5: Discussion

5.1 Major Findings

The main finding of the current study is that WBV, when compared to PS without vibration, did not cause a change in aortic, leg or arm PWV in individuals with SCI. A second major finding is the demonstration that measuring aortic PWV in people with SCI has a high intra- and inter-observer reliability and therefore can be used with confidence when assessing arterial compliance.

Furthermore, when grouped based on level and severity of injury, there were no differences found when comparing PWV after WBV and PS. However there was a trend for those with SCI below T5 to have the leg PWV rise seen in PS attenuated with the addition of WBV. There was a trend for a positive correlation that showed that the shorter the time post-injury, the greater the decrease in PWV.

Many studies have shown that people with SCI have an increased risk for cardiovascular disease (DeVivo et al., 1999; Krassioukov et al., 2003). Miyatani et al., (2009) demonstrated that PWV, an index of arterial stiffness, is increased in people with SCI, and this increased stiffness, or reduced arterial compliance, has been reported to be an independent cardiovascular risk factor (Arnett et al., 1994). Exercise has been shown to improve arterial compliance and improve cardiovascular conditioning in the able-bodied population (Vaitkevicius et al., 1993; Tanaka et al., 2000; Otsuki et al., 2007; Heffernan et al., 2007; Maeda et al., 2008). As there are many challenges for exercise in individuals with SCI, other modalities have been investigated in an effort to improve their cardiovascular health. Both acute and long-term WBV, have been shown to have a positive effect on both muscle strength (Mester et al., 2006; Roelants et al., 2007;

Bogaerts et al., 2009) and cardiac conditioning in the able-bodied population (Rittweger et al., 2001, Yamada et al., 2008). Furthermore, a study by Otsuki et al., (2008) demonstrated a reduction of PWV in able-bodied individuals after an acute bout of WBV. The current study aimed to investigate if an acute session of WBV would reduce the PWV in people with SCI.

The current study was the first to examine the effects of an acute bout of WBV on PWV in individuals with SCI with the hypothesis that there would be a reduction in PWV and improved arterial compliance after the acute bout of WBV. However, after the acute bout of WBV, no change was observed in the aorta, leg or arm PWV in all the participants regardless of the level or severity of injury. The response to an acute bout of WBV varied highly between participants, and characteristics specific to SCI did not have a significant influence on the effects of WBV. These results were not anticipated and were in contrast to the study of Otsuki et al. (2008).

There are several possible factors that may explain the lack of expected outcomes in this study. The mechanisms are related to the specific characteristics of the individuals with SCI well as several methodological parameters.

The reduced effects of the WBV may be related specifically to the spinal cord injury. One mechanism for the reduction of PWV by WBV is thought to be through the exercise conditioning effect of the muscle contractions induced by the tonic vibration reflex (Rittweger, 2010). In people with SCI above T5 there is disruption of the sympathetic nervous system and consequent reduced cardiac response to meet the demands of increased muscle work (Teasel et al., 2000). This would be a potential explanation of the lack of response in the higher level SCI individuals. However, there

was no effect of WBV regardless of level of injury and another explanation is needed. It is thought that the tonic vibration reflex acts via the stretch reflex of the muscle spindles (Rittweger, 2010). After a SCI there is muscle atrophy with shortening and changes in composition of the muscle fibers and spindles. This may cause a reduced sensitivity for the muscle spindles to fire. As a result there is the potential for less spindle firing and muscle contraction response to the vibration. Thus, individuals with SCI may have a smaller muscle contraction response with less of a cardiac exercise-induced conditioning effect. As well, with reduced muscle contraction activation from the TVR there will be a reduced increase in local blood flow in the muscles, a reduced vessel wall deformation and reduced increase in limb vessel compliance.

The lack of reduction in PWV in both individuals with complete or incomplete injuries may be related to the lack of background muscle activity needed for the summation with the TVR to produce significant muscle contractions. In Otsuki *et al.* (2008), the participants were in a static squat on the vibrating platform. This is to say that they were actively standing in a posture against gravity that demanded muscle activity to maintain the position. The participants in the present study, due to the nature of their injury, would have difficulty or would be incapable of performing a static squat, or indeed any active standing on their own. As a result of being held in a passive stance there was a lack of the background muscle activity that is required for the tonic vibration stretch reflex to summate with, and stimulate increased muscle activation. As mentioned in Cochrane *et al.* (2008), a Jendrassik maneuver was necessary to activate the muscles prior to WBV to show any cardiovascular response. Therefore, passively standing during WBV, as in the current protocol, may have reduced the cardiovascular effect that has

been seen in the literature. As well, this lack of background muscle activity, which would have reduced the leg muscle contraction response, would potentially reduce the WBV effect on the leg arterial compliance changes.

The strength of the vibration from the vibrating platform may also have been a limiting factor in the present study. As the vibration travels more proximally from the feet, the strength of the vibration is reduced (Rees *et al.*, 2008). In addition, the angle of knee and hip flexion are determining factors as to how high the vibration travels within the body (Rittweger, 2010). While standing fully erect, or nearly erect, with knees locked in extension, the vibration is transferred to the upper body, which may cause discomfort due to the shaking of the head and eyes (Rees *et al.*, 2008). Therefore, with individuals being placed in a squatting position where the weight is posed on the forefoot, the resonance of the vibration is dissipated in the abdomen thus minimizing the discomfort individuals experienced (Rittweger, 2010). The present protocol required participants to stand with the knees at near full extension which may have permitted the vibration to travel up the body to the head. With the knees extended, it may have been more likely for the vibration-compression effect to act on the abdominal and thoracic aorta which, in turn, would increase the potential for aortic vessel deformation and improved compliance. However, due to the vibration effects on the head, the amplitude of the vibration was kept at 0.6 mm to reduce the discomfort. This amplitude was in contrast to the amplitude of Otsuki *et al.* (2008) which was 2-4mm. Therefore the strength of the vibration in this study may have been insufficient to attain the desired effect on the activation of the muscle contractions as well as on the shearing of the blood vessels. As such, there was not the expected increase in arterial compliance and reduced PWV. It is

of interest to note that there was a trend in the leg PWV change such that the increase seen in PWV following PS was reduced with the addition of the WBV. It is possible that the strength of the vibration in this study protocol with the knees extended was higher in the lower extremities than the strength of the vibration arriving at the aorta. As such, there was a lowering of the PWV with the WBV compared to the PS alone.

5.2 Clinical Significance

As the present results indicate, PWV did not change following acute WBV. As such, it may not be a feasible method for reducing arterial stiffness and consequently morbidity and mortality associated with CVD. However, several factors have been clearly indicated that may have played a role in the lack of significant findings. Because people with SCI have great difficulty engaging many forms of exercise, and have a high risk for CVD, it is imperative to consider certain modifications that can optimize WBV before it is disregarded.

Although there were no changes in the PWV after acute WBV, it would be worthwhile to investigate the long-term effects of WBV on PWV in people with SCI. As the conditioning effects of the muscle contractions are modest, they may accumulate over time if repeated and yield significant clinical value. As well, the repeated deformation of the vessels, although of small amplitude, may accrue over time and result in an increase in arterial compliance. Future studies of long-term WBV are needed to investigate its potential as a form of exercise for people with SCI.

It may be useful to think of the clinical value of WBV in the early adjustment period post-traumatic SCI. A trend was shown for a correlation between time post-injury and change in aortic PWV after WBV. The trend indicated that the more acute the injury,

the greater the decrease in PWV following WBV. This may indicate that if WBV is introduced within the first year or so post-injury, when the muscle atrophy is less marked, it may confer a greater response in reducing PWV. As aortic PWV is an important indicator of arterial stiffness associated with cardiovascular morbidity, the implementation of WBV as soon as medically permitted post-injury may help reduce the cardiovascular risk.

As shown in the able-bodied population (Lehmann *et al.*, 1992; Naidu *et al.*, 2005; Lee *et al.*, 2009 and Frimodt-Moller *et al.*, 2008), the current study showed a high intra-and inter-observer reliability for PWV analysis after SCI. As such, PWV can be confidently used as a tool for assessing aortic stiffness. The intra- and inter-observer reliability for PWV in individuals with SCI had never been tested. The current study showed that the inter-observer interclass correlation coefficient was 0.76 ($p=0.006$). According to Landis and Koch (1977), this correlation coefficient is 'good' as it falls between 0.60 and 0.81. The current study showed that the intra-observer interclass correlation coefficient was 0.93 ($p<0.001$). According to Landis and Koch (1977), this correlation coefficient is 'excellent' as it is above 0.81. The Bland-Altman graphs show that each point falls within $\pm 2SD$ for inter- and intra-observer reliability. In addition, there is no skewness to the graphs meaning the difference between the observers and within observer, is not dependent on the magnitude of the PWV value calculated. As such, and similarly to the able-bodied population, PWV can be reliably analyzed both within and between testers for the SCI population.

5.3 Limitations

Certain limitations existed in the current study. First, due to the paralysis that accompanies SCI, a standing apparatus was necessary in order for the participants to be upright on the vibrating platform for the duration of the protocol. The participants had a portion of their weight on a back seat (in addition to the heels of their feet) and therefore the use of the standing frame provided full support for a passive stance and there was no active muscle contraction performed by the participants.

Secondly, the participants were lifted to a knee angle of 160° , whereas 180° is full knee extension. As previously mentioned, the closer the knee is to full extension, the more discomfort the participant experiences due to the transmission of the vibration to the head. In fact, several participants did complain of bothersome discomfort such as shaking and buzzing at the head. To alleviate this head shaking, participants tended to take more of their weight through their arms on the arm rest which may have reduced the vibration through the legs to the abdomen. Furthermore, the discomfort of transmission of the vibration up to the head may have been a factor that limited the amplitude of the vibration that could be tolerated, and therefore, the amplitude and frequency of vibration employed in the present study were different than those employed in Otsuki *et al.*, (2008).

Lastly, as individuals with SCI have different injury characteristics (ie. level and severity of injury) it is difficult to make group comparisons with a total population of 8 participants. Trends were seen for a difference in baseline leg ($p=0.07$) and arm ($p=0.06$) PWV when comparing those with injuries above and below T5. That is, there was a trend for a higher baseline PWV in the arm and leg in those with an injury below T5. The effect size for this difference was moderate, and therefore increasing the sample size may

lead to statistical significance. This evidence combined with the lower rise in PWV in the leg after the WBV compared to the PS in the individuals with injuries below T5, may indicate that the WBV may have had a greater effect on the more stiffer. This finding gives some support to the value of WBV in improving arterial compliance. It is possible that with modifications in the protocol, and a larger and more homogeneous sample, the positive effect of WBV on reducing the PWV (and therefore increasing arterial compliance) would be observed. As well, we did not assess the activity habits of our participants. Individuals who are more physically active will have more conditioned muscles, which may ultimately have the potential for a stronger response to the stretch of the vibration. In addition, those who are more physically active will have a more conditioned cardiovascular system and may respond better to the vibration exercise. As seen in Maeda *et al.*, (2008), acute endurance exercise did not cause an increase in arterial compliance before training. However, after training, there was a significant increase in compliance following an acute bout of exercise.

Chapter 6: Future Research and Conclusions

6.1 Future Research

This study was the first study to investigate the acute effect of WBV on arterial stiffness as assessed by PWV in individuals with SCI. For that reason, it may serve as a building block for many possible and exciting new research ideas that may benefit this vulnerable population. A long-term training protocol would be useful to determine whether WBV over a prolonged period of time will have a positive effect on arterial compliance. It would also be beneficial to have more homogenous groups and a large number of participants that would allow for a more thorough control of time post-injury, physical activity levels, the level and severity of injury, and lower limb strength. Increasing the participant pool for specific groups will help to distinguish which groups of individuals with SCI may benefit more from an acute and/or long-term protocol of WBV.

Future research can also be conducted with a slightly refined methodology. First, it would be beneficial to have the participants undergo WBV with some knee flexion to reduce the vibrations from travelling up to the head. This would lessen the discomfort felt by the participants so that the more intense parameters of 26 Hz and 2mm amplitude, that has been used by others could be employed (Ostuki *et al.*, 2008). Furthermore, there may be some benefit from increasing the "on" time duration of the vibration stimulation to provide a potentially greater strength of vibration stimulus on the muscles and vessels. The increased strength of the vibration stimulus would have the potential to more greatly affect vessel deformation and increase arterial compliance.

Another protocol modification that may yield better results would be for the use

of a bodyweight support in conjunction with WBV so that the participants would be able to maintain as much of an active posture against gravity as possible. The WBV effects may be optimized as a result of more muscle recruitment during vibration. Furthermore, individuals with incomplete or complete injuries who are unable to stand on their own may benefit from performing a Jendrassik maneuver for a general whole-body muscle excitation (at least to all the innervated muscles) which may confer a greater response to WBV. Increasing muscle activity during vibration may cause a higher muscle contraction strength response which in turn, may improve the general conditioning effect on the cardiac system and result in the reduced PWV of the vessels.

6.2 Conclusions

The present study was the first to examine the acute effect of WBV on PWV in individuals with SCI. The results showed that PWV was not changed following WBV and therefore WBV may not be an effective form of exercise to reduce the cardiovascular risk associated with increased arterial stiffness. It was also noted that neither baseline PWV, nor the change in PWV with WBV, varied based on the level or severity of injury. There may have been certain aspects of the protocol that may have contributed to the lack of change. Therefore, WBV must not be disregarded as a form of exercise intervention to help reduce the risk of CVD within this population. Rather, future studies with protocol modifications must be examined.

This study was also the first to examine inter- and intra-observer reliability for PWV in individuals with SCI. The results showed that PWV is a reliable assessment tool and can be used with confidence in individuals with SCI.

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Figures

Aortic PWV following PS and WBV in Individuals with SCI.

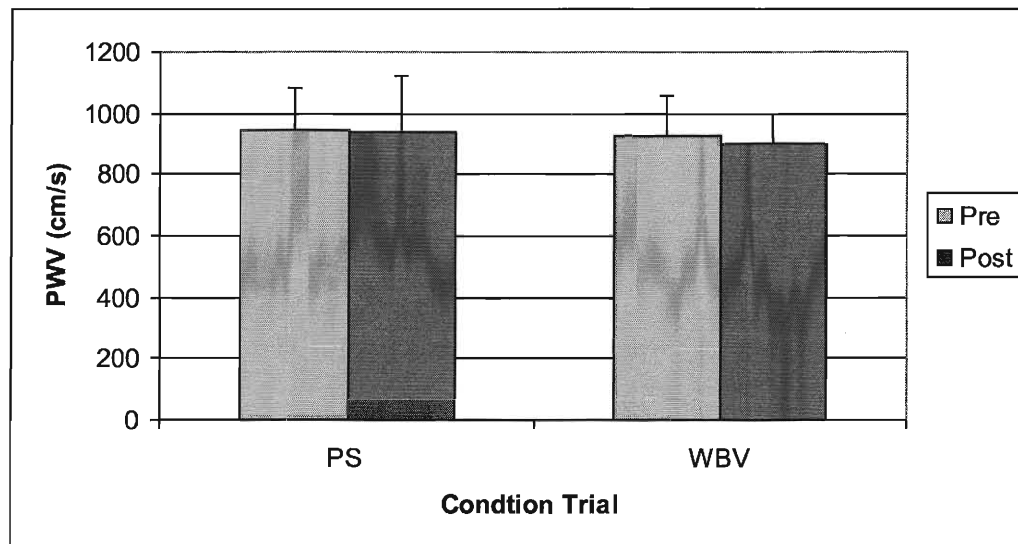


Figure 5: Aortic PWV before and after PS and WBV in individuals with SCI. PWV values are expressed as means \pm SD. Significance was set at $p \leq 0.05$.

Leg PWV following PS and WBV in Individuals with SCI.

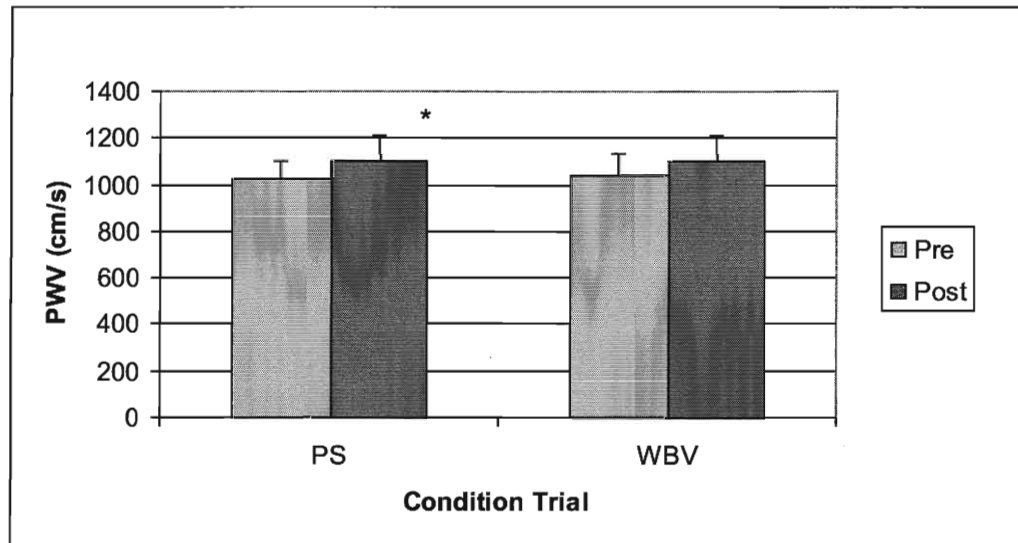


Figure 6: Leg PWV before and after PS and WBV in individuals with SCI. PWV values are expressed as means \pm SD. Significance was set at $p \leq 0.05$. * denotes significant change from pre- to post- PS as determined by 1-way ANOVA only.

Arm PWV following PS and WBV in Individuals with SCI

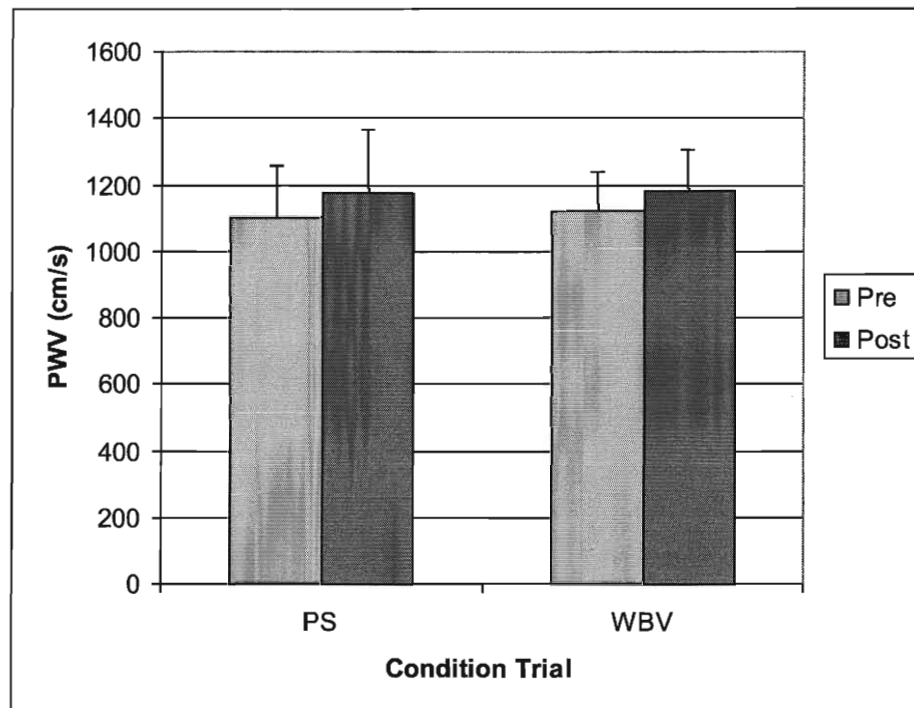


Figure 7: Arm PWV before and after PS and WBV in individuals with SCI. PWV values are expressed as means \pm SD. Significance was set at $p \leq 0.05$.

Aortic PWV following PS and WBV in Individuals with an Injury Above T5

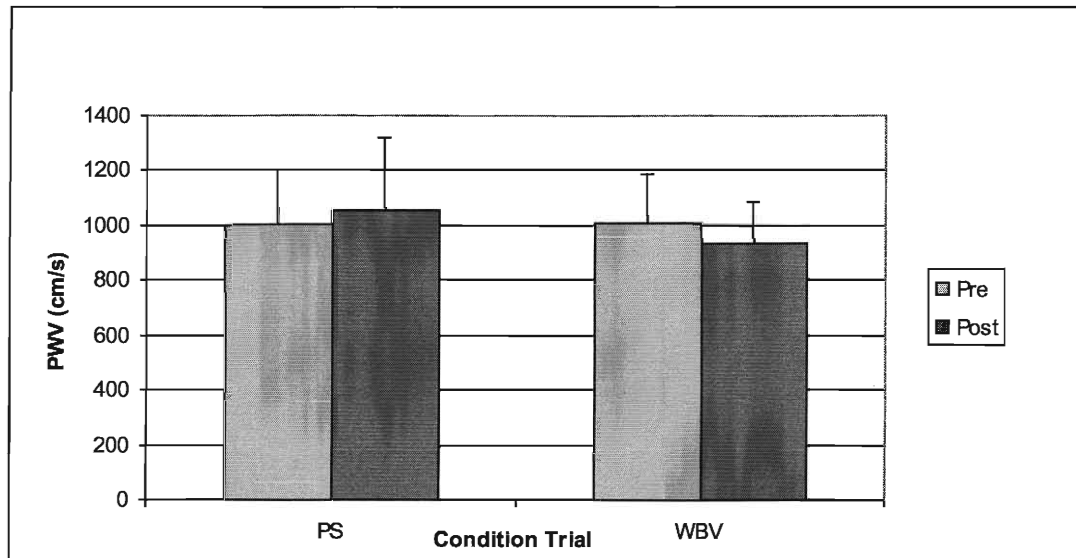


Figure 8: Aortic PWV before and after PS and WBV in individuals with an injury above T5. PWV values are expressed as means \pm SD. Significance was set at $p \leq 0.05$.

Aortic PWV following PS and WBV in Individuals with an Injury Below T5

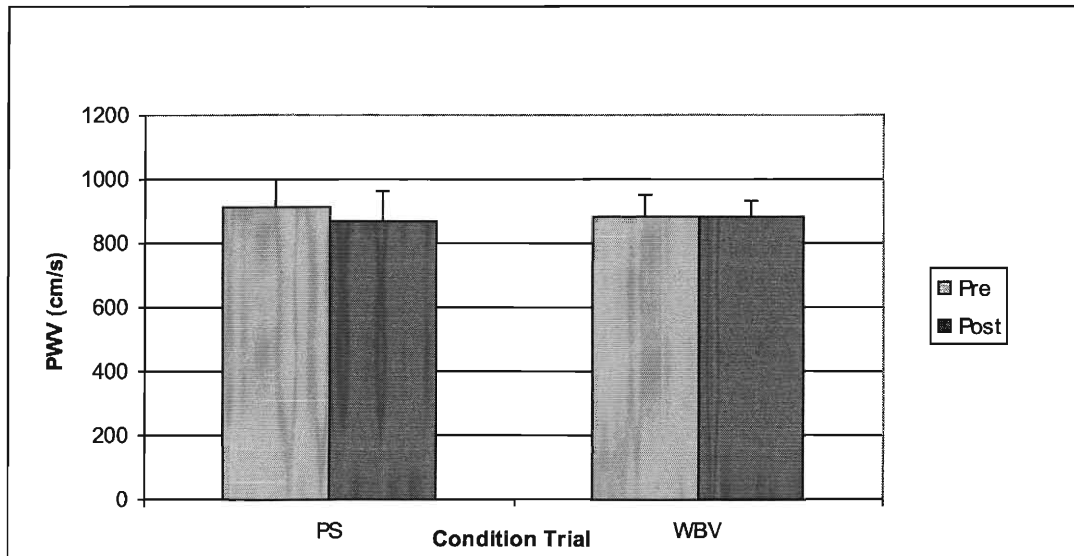


Figure 9: Aortic PWV before and after PS and WBV in individuals with an injury below T5. PWV values are expressed as means \pm SD. Significance was set at $p \leq 0.05$.

Leg PWV following PS and WBV in Individuals with an Injury Above T5

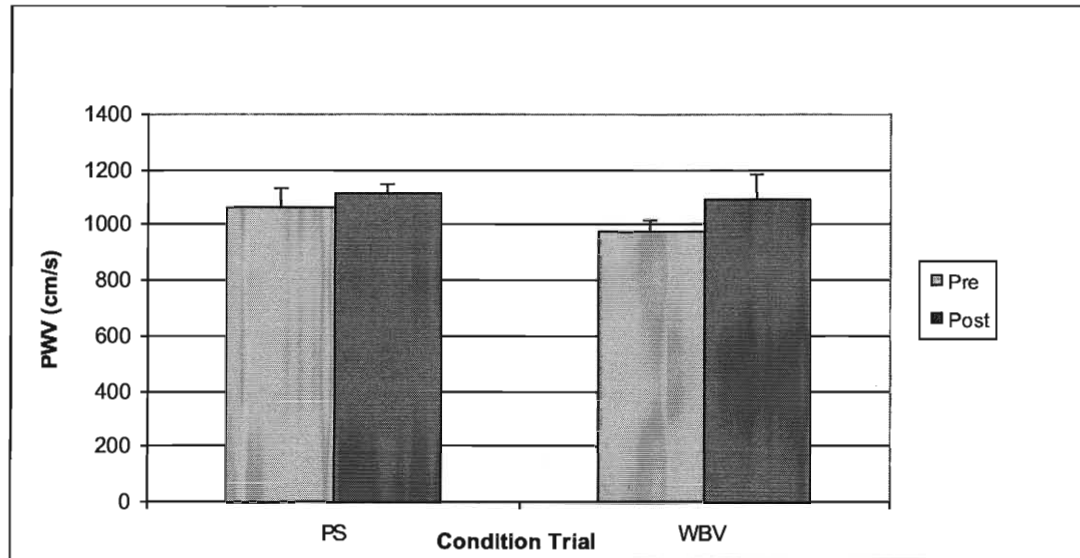


Figure 10: Leg PWV before and after PS and WBV in individuals with an injury above T5. PWV values are expressed as means \pm SD. Significance was set at $p \leq 0.05$.

Arm PWV following PS and WBV in Individuals with an Injury Above T5

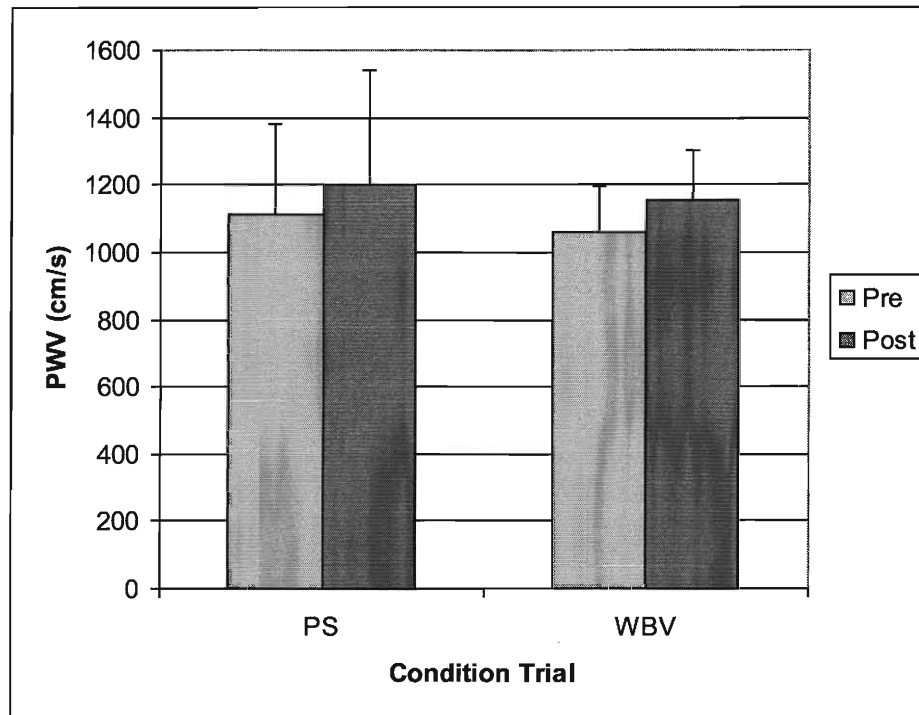


Figure 11: Arm PWV before and after PS and WBV in individuals with an injury above T5. PWV values are expressed as means \pm SD. Significance was set at $p \leq 0.05$.

Leg PWV following PS and WBV in Individuals with an Injury Below T5

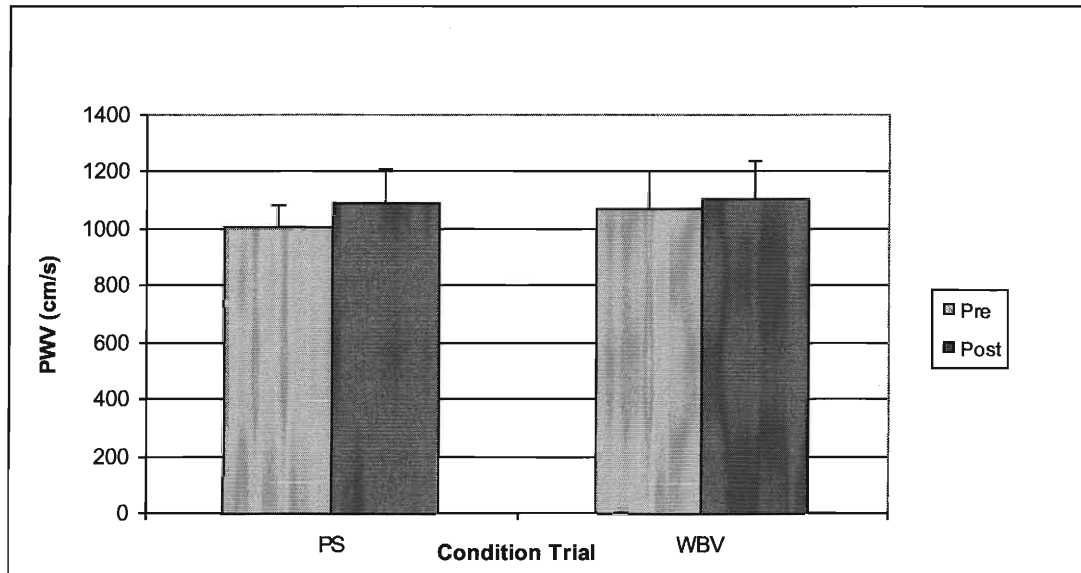


Figure 12: Leg PWV before and after PS and WBV in individuals with an injury below T5. PWV values are expressed as means \pm SD. Significance was set at $p \leq 0.05$.

Arm PWV following PS and WBV in Individuals with an Injury Below T5

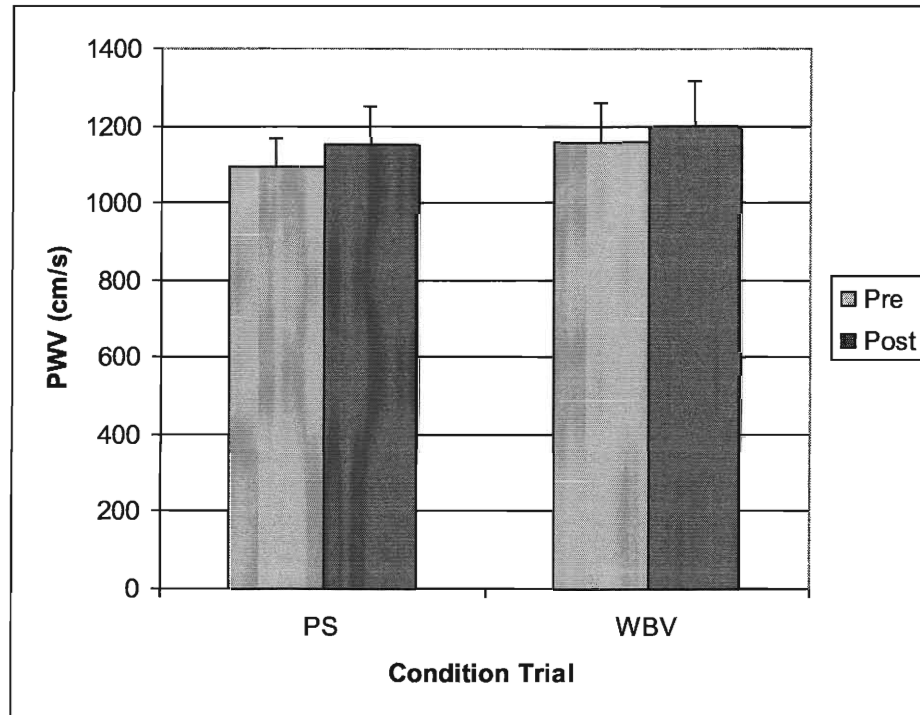


Figure 13: Arm PWV before and after PS and WBV in individuals with an injury below T5. PWV values are expressed as means \pm SD. Significance was set at $p \leq 0.05$.

Aortic PWV following PS and WBV in Individuals with a Complete Injury

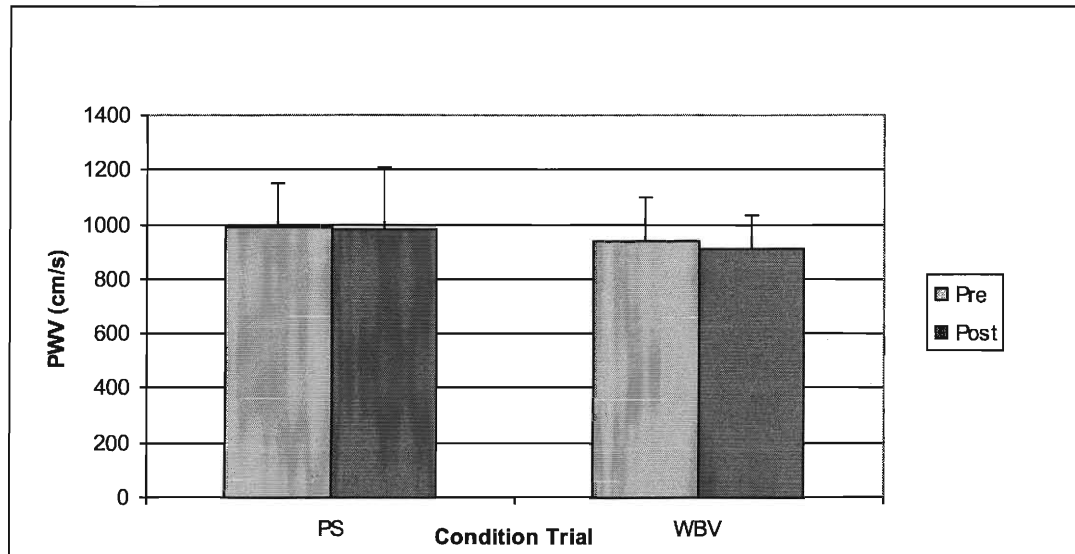


Figure 14: Aortic PWV before and after PS and WBV in individuals with a complete injury. PWV values are expressed as means \pm SD. Significance was set at $p \leq 0.05$.

Aortic PWV following PS and WBV in Individuals with an Incomplete Injury

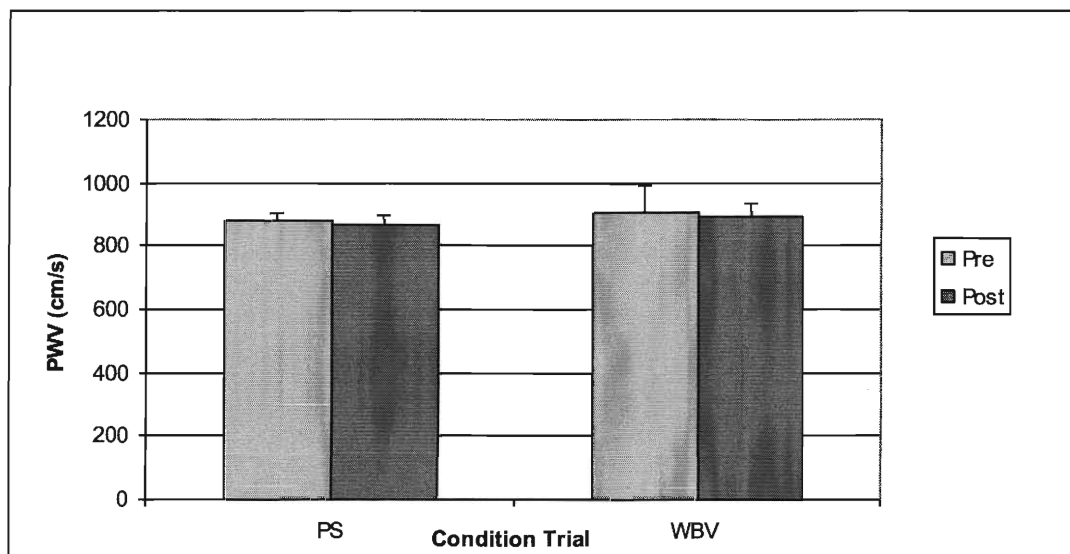


Figure 15: Aortic PWV before and after PS and WBV in individuals with an incomplete injury. PWV values are expressed as means \pm SD. Significance was set at $p \leq 0.05$.

Leg PWV following PS and WBV in Individuals with a Complete Injury

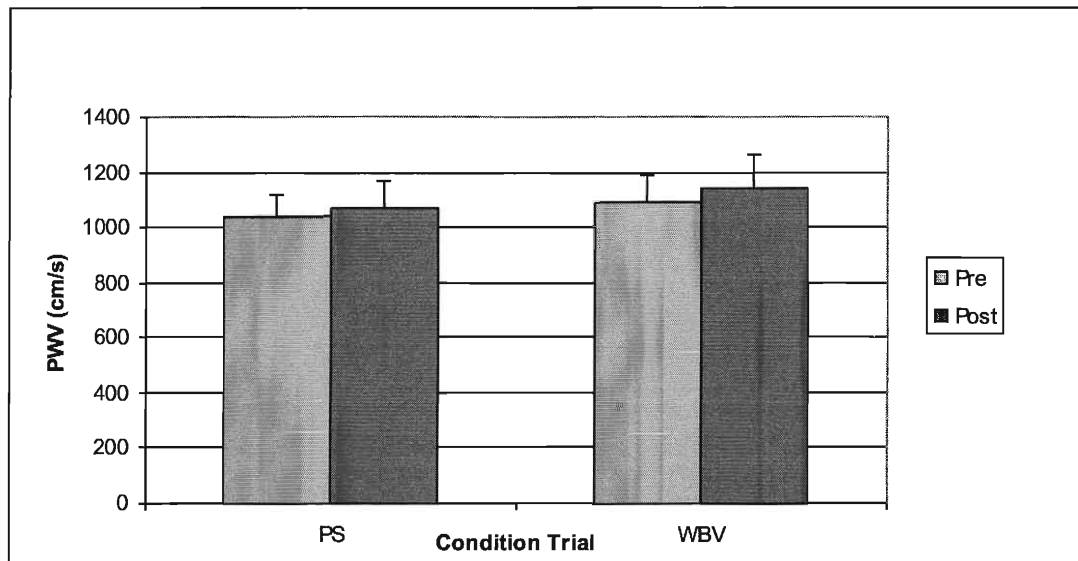


Figure 16: Leg PWV before and after PS and WBV in individuals with a complete injury. PWV values are expressed as means \pm SD. Significance was set at $p \leq 0.05$.

Arm PWV following PS and WBV in Individuals with a Complete Injury

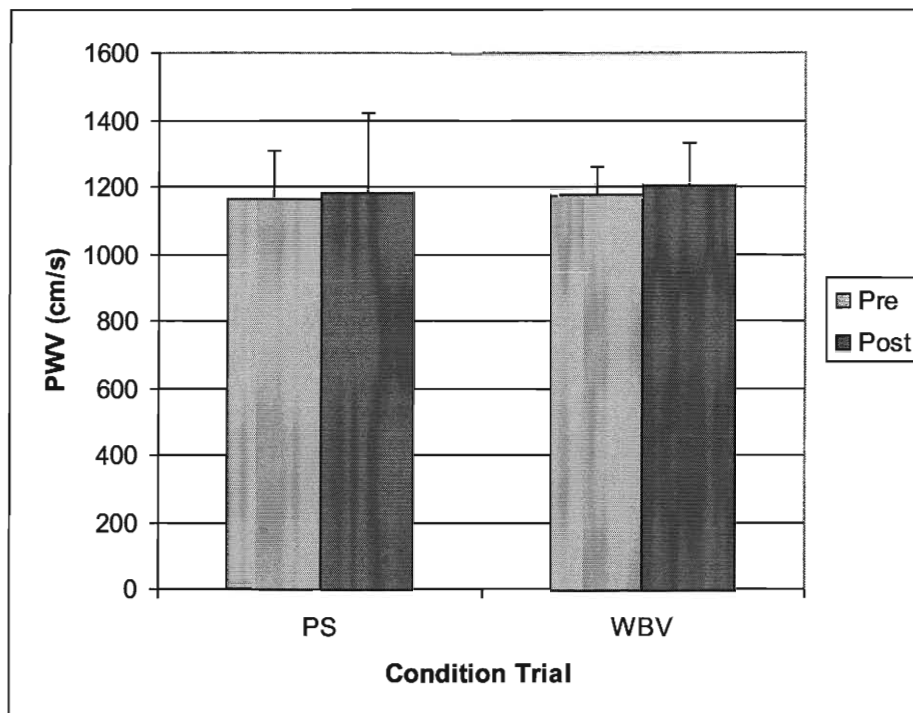


Figure 17: Arm PWV before and after PS and WBV in individuals with a complete injury. PWV values are expressed means \pm SD. Significance was set at $p \leq 0.05$.

Leg PWV following PS and WBV in Individuals with an Incomplete Injury

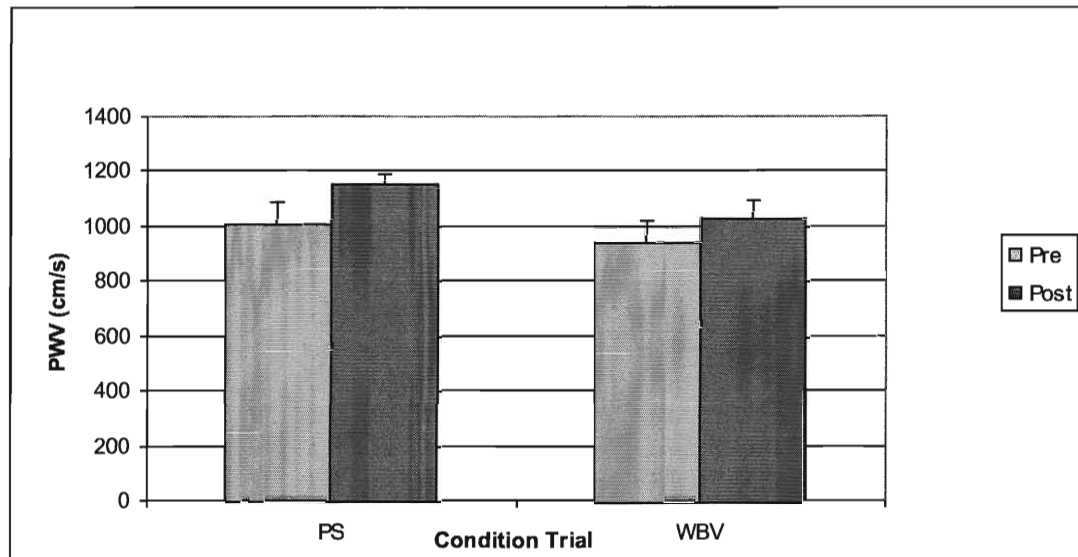


Figure 18: Leg PWV before and after PS and WBV in individuals with an incomplete injury. PWV values are expressed as means \pm SD. Significance was set at $p \leq 0.05$.

Arm PWV following PS and WBV in Individuals with an Incomplete Injury

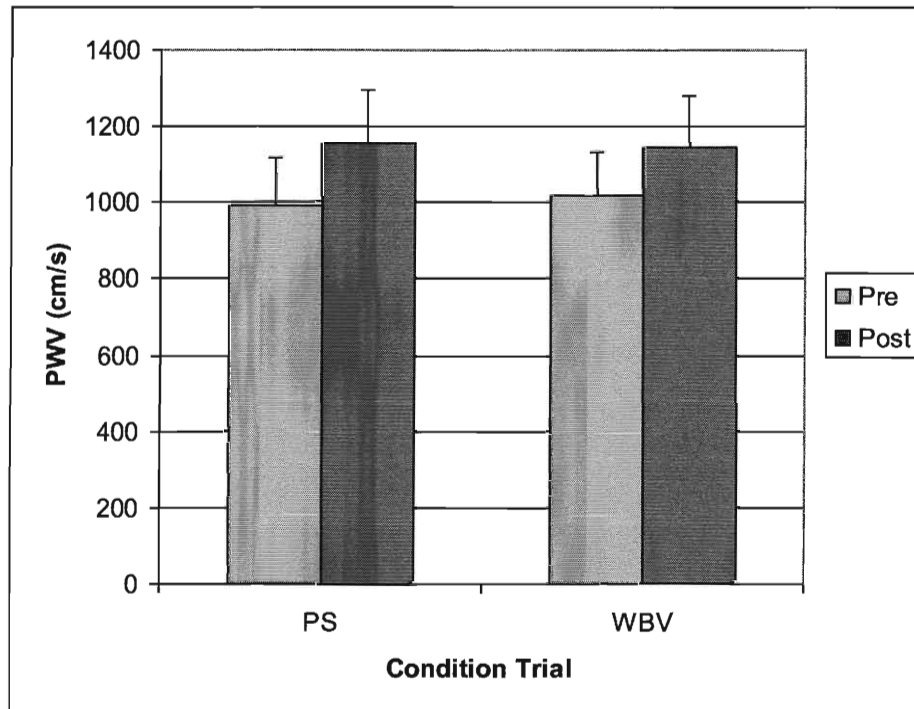


Figure 19: Arm PWV before and after PS and WBV in individuals with an incomplete injury. PWV values are expressed as means \pm SD. Significance was set at $p \leq 0.05$.

Aortic PWV Following PS and WBV Normalized for Baseline PWV Values in Individuals with SCI

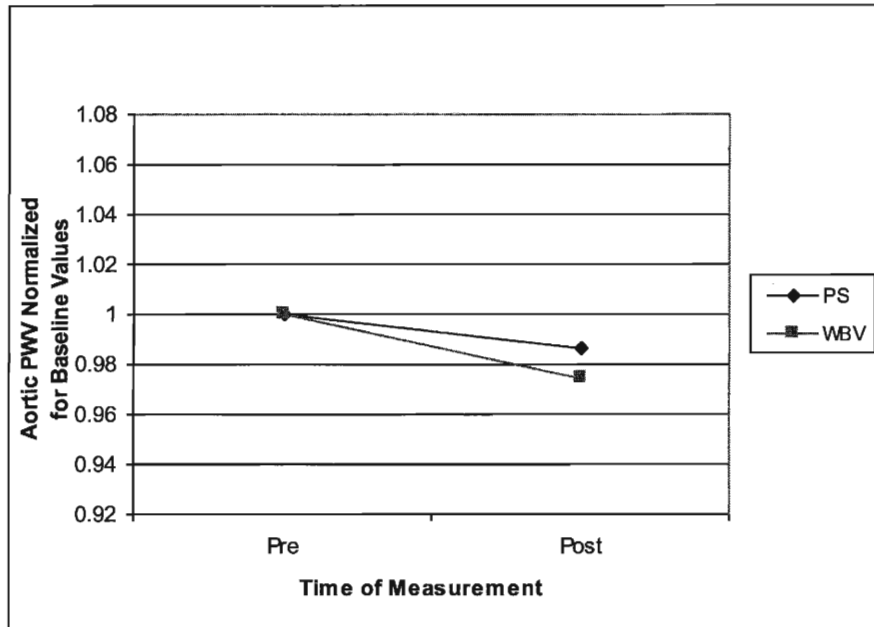


Figure 20: Aortic PWV before and after PS and WBV normalized for baseline PWV values in individuals with SCI. Values are expressed as a percent change from baseline value. Significance was set at $p \leq 0.05$.

Leg PWV Following PS and WBV Normalized for Baseline PWV Values in Individuals with SCI

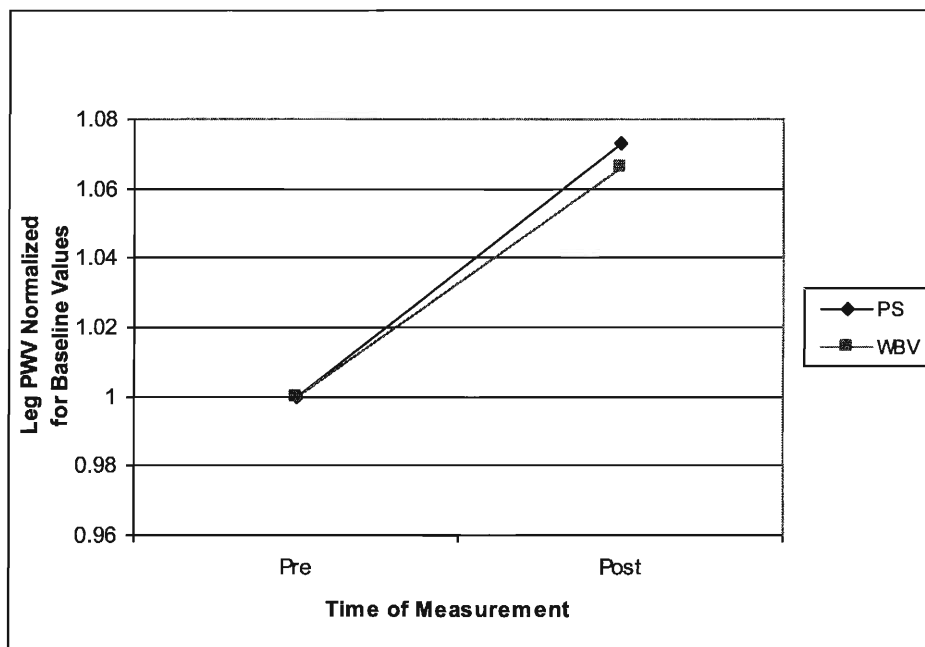


Figure 21: Leg PWV following PS and WBV normalized for baseline PWV values in individuals with SCI. Values are expressed as a percent change from baseline value. Significance was set at $p \leq 0.05$.

Arm PWV Following PS and WBV Normalized for Baseline PWV Values in Individuals with SCI

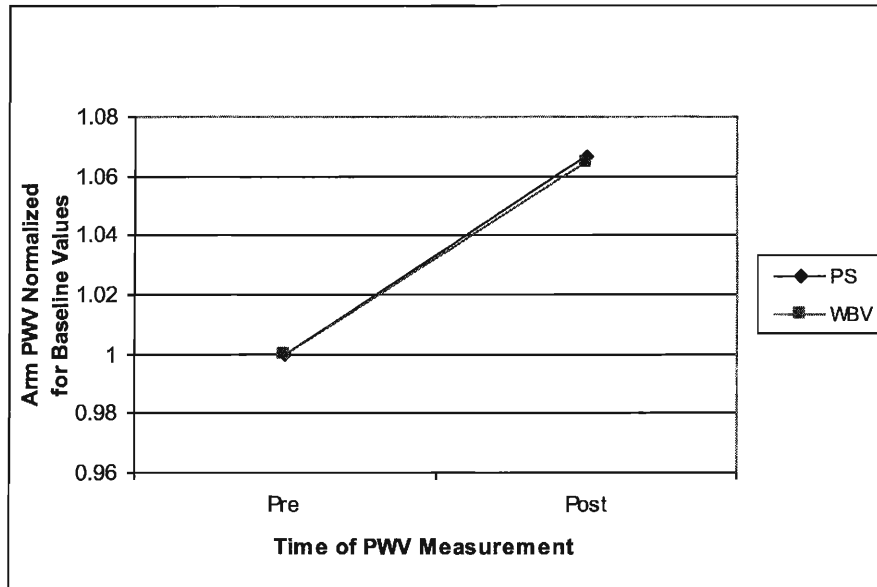


Figure 22: Arm PWV following PS and WBV normalized for baseline PWV values in individuals with SCI. Values are expressed as a percent change from baseline value. Significance was set at $p \leq 0.05$.

Baseline Aortic PWV Grouped For Level of Injury

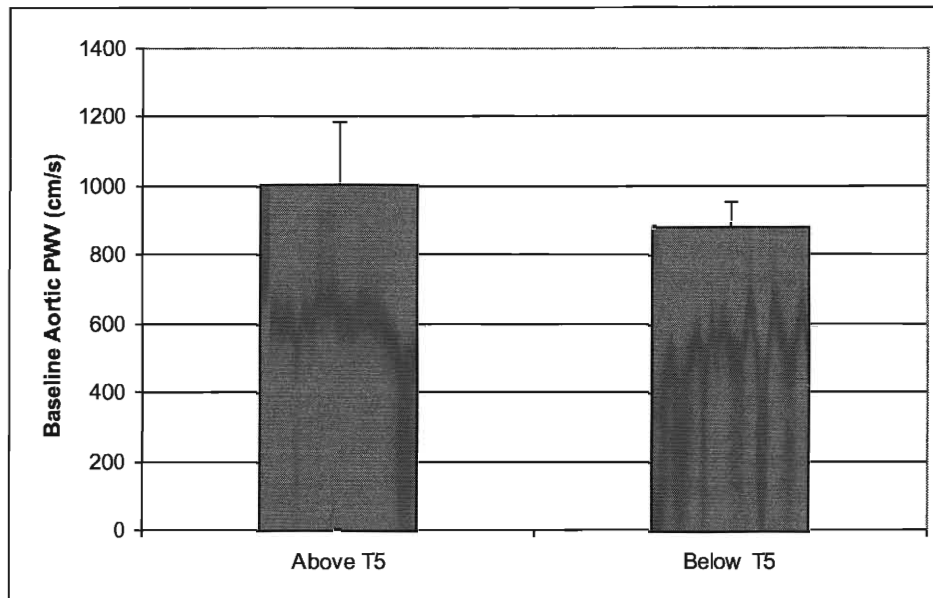


Figure 23: Differences between baseline aortic PWV when grouped for injuries above or below T5. PWV values are expressed as means \pm SD. Significance was set at $p \leq 0.05$.

Baseline Leg PWV Grouped For Level of Injury

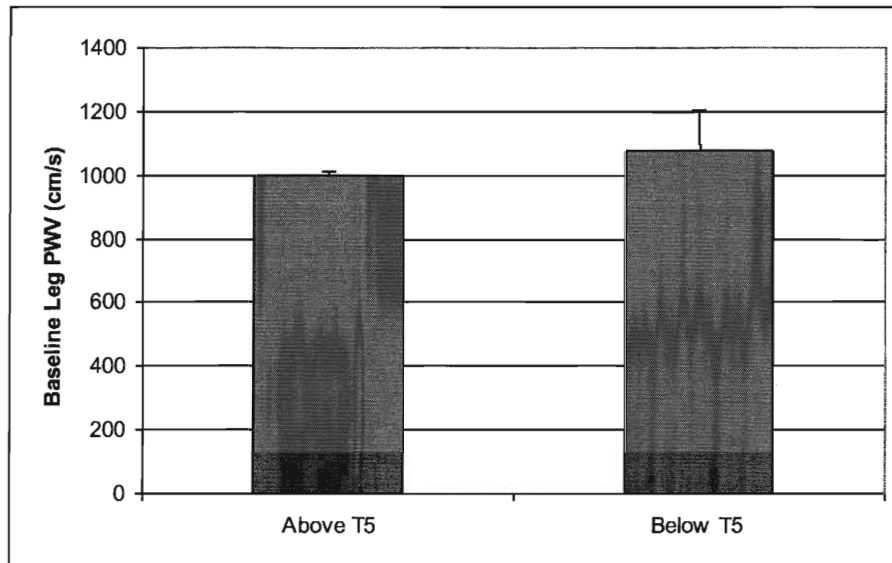


Figure 24: Differences between baseline leg PWV when grouped for injuries above or below T5. PWV values are expressed as means \pm SD. Significance was set at $p \leq 0.05$.

Baseline Arm PWV Grouped For Level of Injury

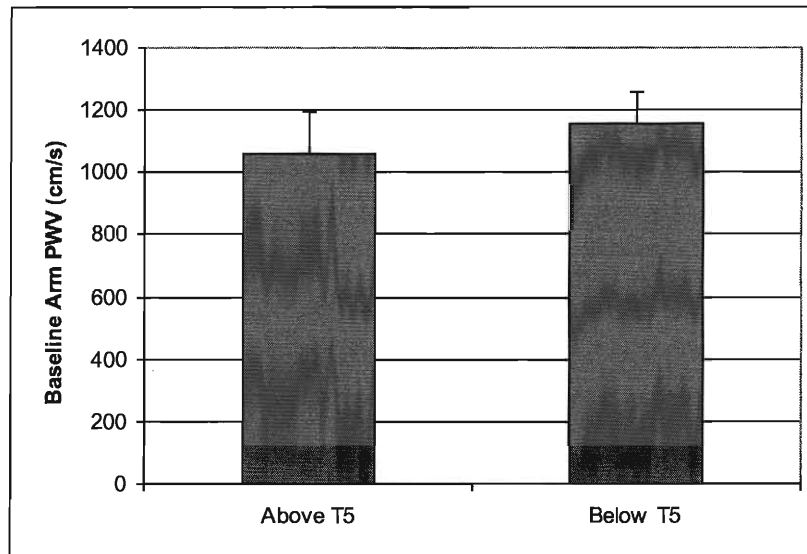


Figure 25: Differences between baseline arm PWV when grouped for injuries above or below T5. PWV values are expressed as means \pm SD. Significance was set at $p \leq 0.05$.

Baseline Aortic PWV Grouped For Severity of Injury

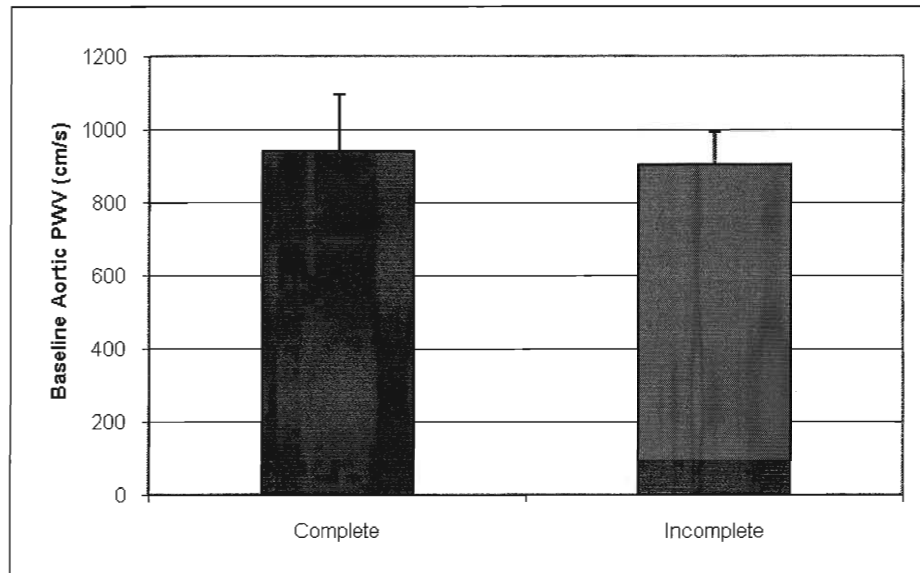


Figure 26: Differences between baseline aortic PWV when grouped for complete or incomplete injuries. PWV values are expressed as means \pm SD. Significance was set at $p \leq 0.05$.

Baseline Leg PWV Grouped For Severity of Injury

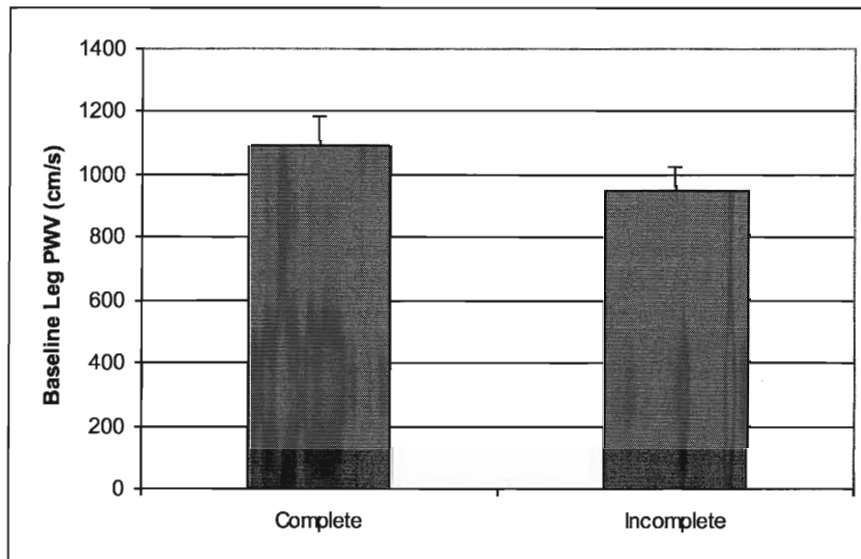


Figure 27: Differences between baseline leg PWV when grouped for complete or incomplete injuries. PWV values are expressed as means \pm SD. Significance was set at $p \leq 0.05$.

Baseline Arm PWV Grouped For Severity of Injury

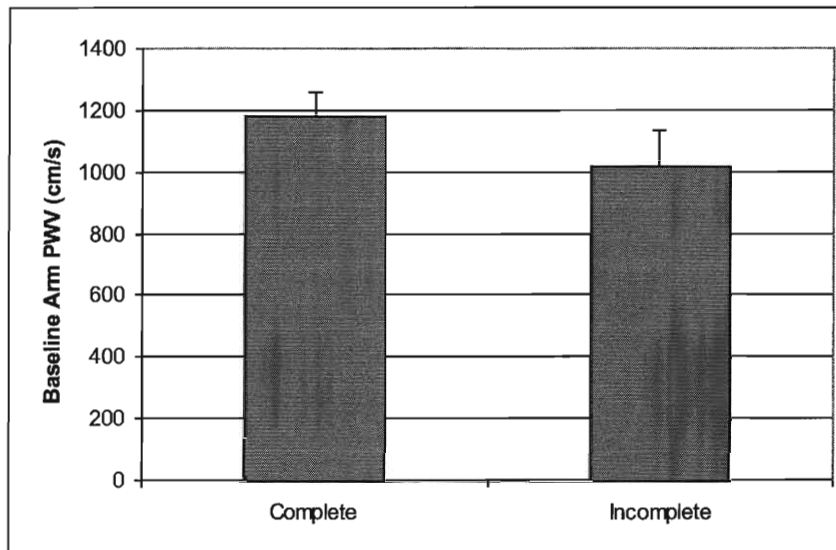
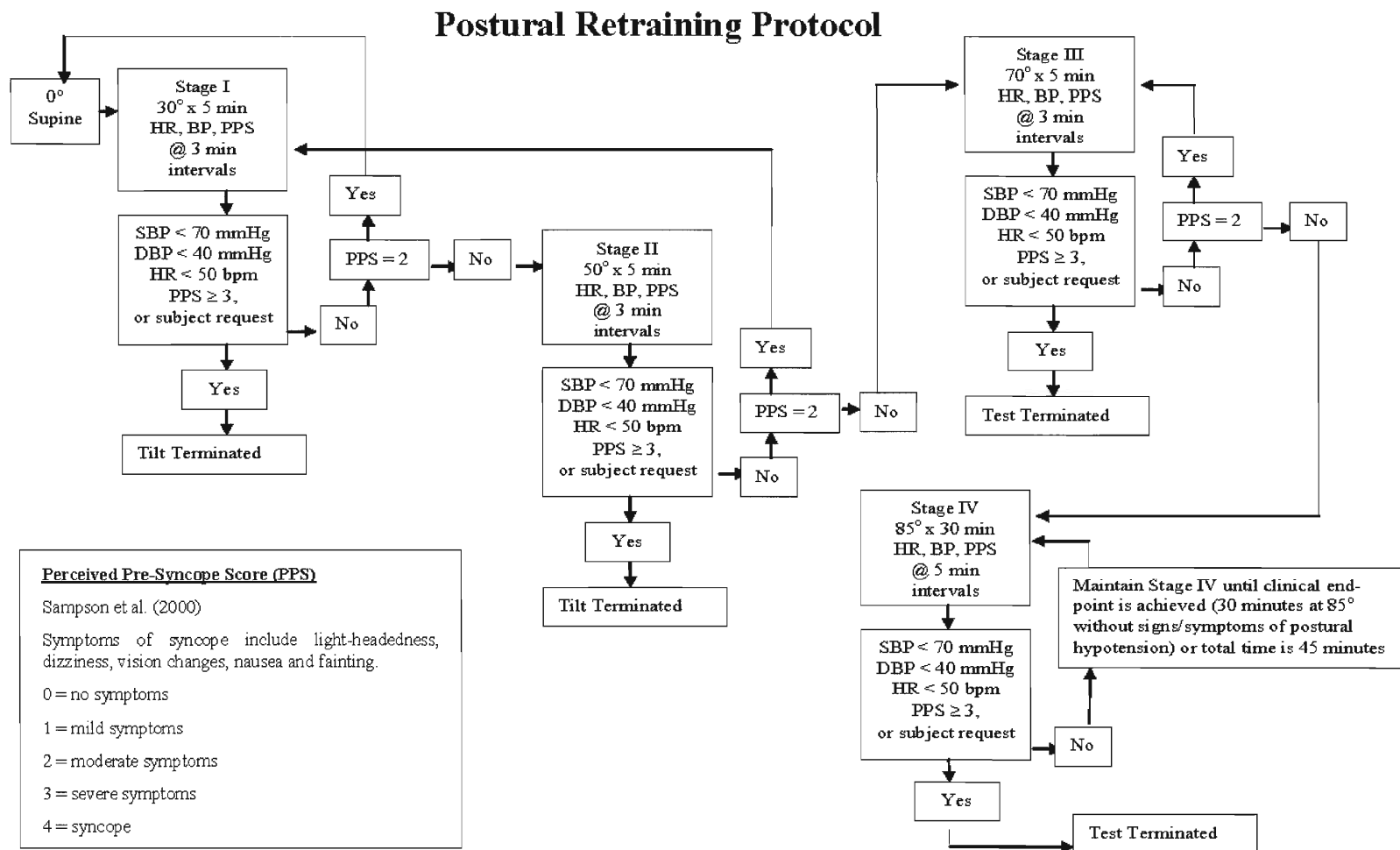


Figure 28: Differences between baseline arm PWV when grouped for complete or incomplete injuries. PWV values are expressed as means \pm SD. Significance was set at $p \leq 0.05$.

Appendices

Appendix A: Postural Retraining Protocol



Note: First training session begins at Stage 1. If successive training sessions are needed, begin at the last completed stage (i.e., stage maintained for 15 minutes and PPS<2). The maximum number of training sessions is five.

Appendix B: Standard Neurological Classification of Spinal Cord Injury

Patient Name _____

Examiner Name _____ Date/Time of Exam _____



STANDARD NEUROLOGICAL CLASSIFICATION OF SPINAL CORD INJURY



MOTOR

KEY MUSCLES
(scoring on reverse side)

	R	L	
C5	<input type="checkbox"/>	<input type="checkbox"/>	Elbow flexors
C6	<input type="checkbox"/>	<input type="checkbox"/>	Wrist extensors
C7	<input type="checkbox"/>	<input type="checkbox"/>	Elbow extensors
C8	<input type="checkbox"/>	<input type="checkbox"/>	Finger flexors (distal phalanx of middle finger)
T1	<input type="checkbox"/>	<input type="checkbox"/>	Finger abductors (little finger)

UPPER LIMB TOTAL (MAXIMUM) ☐ + ☐ = ☐
(25) (25) (50)

Comments:

L2	<input type="checkbox"/>	<input type="checkbox"/>	Hip flexors
L3	<input type="checkbox"/>	<input type="checkbox"/>	Knee extensors
L4	<input type="checkbox"/>	<input type="checkbox"/>	Ankle dorsiflexors
L5	<input type="checkbox"/>	<input type="checkbox"/>	Long toe extensors
S1	<input type="checkbox"/>	<input type="checkbox"/>	Ankle plantar flexors

Voluntary anal contraction (Yes/No) ☐

LOWER LIMB TOTAL (MAXIMUM) ☐ + ☐ = ☐
(25) (25) (50)

LIGHT TOUCH PIN PRICK

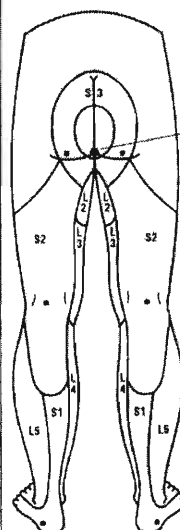
	R	L	R	L
C2				
C3				
C4				
C5				
C6				
C7				
C8				
T1				
T2				
T3				
T4				
T5				
T6				
T7				
T8				
T9				
T10				
T11				
T12				
L1				
L2				
L3				
L4				
L5				
S1				
S2				
S3				
S4-5				

TOTALS { ☐ + ☐ = ☐ }
(MAXIMUM) (56) (56) (56) (56)

SENSORY

KEY SENSORY POINTS

0 = absent
1 = impaired
2 = normal
NT = not testable



Any anal sensation (Yes/No) ☐

PIN PRICK SCORE (max: 112)

LIGHT TOUCH SCORE (max: 112)

NEUROLOGICAL LEVEL
The most caudal segment with normal function

	R	L
SENSORY	<input type="checkbox"/>	<input type="checkbox"/>
MOTOR	<input type="checkbox"/>	<input type="checkbox"/>

COMPLETE OR INCOMPLETE? ☐

Incomplete = Any sensory or motor function in S4-S5

ASIA IMPAIRMENT SCALE

ZONE OF PARTIAL PRESERVATION

Caudal extent of partially innervated segments

	R	L
SENSORY	<input type="checkbox"/>	<input type="checkbox"/>
MOTOR	<input type="checkbox"/>	<input type="checkbox"/>

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REV 03/06

MUSCLE GRADING

- 0 total paralysis
- 1 palpable or visible contraction
- 2 active movement, full range of motion, gravity eliminated
- 3 active movement, full range of motion, against gravity
- 4 active movement, full range of motion, against gravity and provides some resistance
- 5 active movement, full range of motion, against gravity and provides normal resistance
- 5* muscle able to exert, in examiner's judgement, sufficient resistance to be considered normal if identifiable inhibiting factors were not present

NT not testable. Patient unable to reliably exert effort or muscle unavailable for testing due to factors such as immobilization, pain on effort or contracture.

ASIA IMPAIRMENT SCALE

- ☐ **A = Complete:** No motor or sensory function is preserved in the sacral segments S4-S5.
- ☐ **B = Incomplete:** Sensory but not motor function is preserved below the neurological level and includes the sacral segments S4-S5.
- ☐ **C = Incomplete:** Motor function is preserved below the neurological level, and more than half of key muscles below the neurological level have a muscle grade less than 3.
- ☐ **D = Incomplete:** Motor function is preserved below the neurological level, and at least half of key muscles below the neurological level have a muscle grade of 3 or more.
- ☐ **E = Normal:** Motor and sensory function are normal.

CLINICAL SYNDROMES (OPTIONAL)

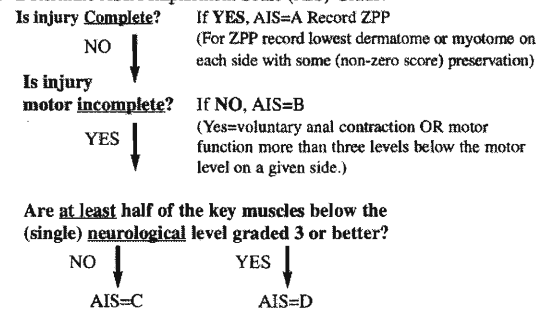
- ☐ Central Cord
- ☐ Brown-Sequard
- ☐ Anterior Cord
- ☐ Conus Medullaris
- ☐ Cauda Equina

STEPS IN CLASSIFICATION

The following order is recommended in determining the classification of individuals with SCI.





- Determine sensory levels for right and left sides.
- Determine motor levels for right and left sides.
Note: in regions where there is no myotome to test, the motor level is presumed to be the same as the sensory level.
- Determine the single neurological level.
This is the lowest segment where motor and sensory function is normal on both sides, and is the most cephalad of the sensory and motor levels determined in steps 1 and 2.
- Determine whether the injury is Complete or Incomplete (sacral sparing).
If voluntary anal contraction = No AND all S4-5 sensory scores = 0 AND any anal sensation = No, then injury is COMPLETE. Otherwise injury is incomplete.

- Determine ASIA Impairment Scale (AIS) Grade:



If sensation and motor function is normal in all segments, AIS=E
Note: AIS E is used in follow up testing when an individual with a documented SCI has recovered normal function. If at initial testing no deficits are found, the individual is neurologically intact; the ASIA Impairment Scale does not apply.

Appendix C: NPUAP Pressure Sore Rating Scale

NATIONAL PRESSURE ULCER ADVISORY PANEL REVISED PRESSURE ULCER STAGING SYSTEM ¹		
Stage/Clinical Presentation	Photo	Pressure Ulcer Definition
		A pressure ulcer is localized injury to the skin and/or underlying tissue, usually over a bony prominence, as a result of pressure or pressure in combination with shear and/or friction. A number of contributing or confounding factors also are associated with pressure ulcers; the significance of these factors is yet to be elucidated.
Stage I: Red heel		<p>Stage I: Intact skin with nonblanchable redness of a localized area, usually over a bony prominence. Darkly pigmented skin may not have visible blanching; its color may differ from the surrounding area</p> <p>Further description: The area may be painful, firm, soft, warmer, or cooler as compared to adjacent tissue. Stage I may be difficult to detect in individuals with dark skin tones. May indicate "at risk" persons (heralding sign of risk)</p>
Stage II: Serous-filled blister		<p>Stage II: Partial-thickness loss of dermis presenting as a shallow open ulcer with a red-pink wound bed, without slough. Also may present as an intact or open/ruptured serum-filled blister</p>
Stage II: Partial-thickness open wound		<p>Further description: Presents as a shiny or dry shallow ulcer without slough or bruising.* This stage should not be used to describe skin tears, tape burns, perineal dermatitis, maceration, or excoriation *Bruising may be a sign of deep tissue injury</p>
Stage III: Full-thickness wound		<p>Stage III: Full-thickness tissue loss. Subcutaneous fat may be visible but bone, tendon, or muscle are not exposed. Slough may be present but does not obscure the depth of tissue loss. May include undermining and tunneling</p> <p>Further description: The depth of a Stage III pressure ulcer varies by anatomical location. The bridge of the nose, ear, occiput, and malleolus do not have subcutaneous tissue and Stage III ulcers can be shallow. In contrast, areas of significant adiposity can develop extremely deep Stage III pressure ulcers. Bone/tendon is not visible or directly palpable</p>

(Fowler *et al.*, 2008)

Appendix D: Raw Data

Table 4: Pulse wave velocity values (cm/s) following PS and WBV measured at the aorta, leg and arm. * denotes a significant change ($p \leq 0.05$).

	PS						WBV					
	Aorta		Leg		Arm		Aorta		Leg		Arm	
Participant	Pre-	Post-	Pre-	Post-	Pre-	Post	Pre-	Post-	Pre-	Post-	Pre-	Post
1	875	878	978	1153	854	1001	997	938	921	1099	917	1066
2	851	887	1093	1188	1092	1294	820	857	1032	1014	1142	1299
3	1044	1020	1061	1205	1181	1037	996	974	1177	1312	1265	1221
4	948	825	1019	1026	1150	1072	847	847	1197	1146	1152	1324
5	815	789	909	913	1023	1185	842	846	1084	1082	1225	1089
6	902	825	938	1118	1031	1159	902	877	874	969	992	1060
7	894	906	1108	1077	1080	1017	829	778	987	1180	1195	1062
8	1237	1361	1092	1101	1395	1592	1190	1088	1009	986	1059	1329
Mean	946	936	1025*	1098*	1101	1170	928	901	1035	1099	1118	1181
SD	136.0	185.3	76.1	94.7	154.8	197.5	127.6	96.5	113.8	114.2	119.8	124.4

Table 5: MAP and HR values before and after PS and WBV

Participant	PS				WBV			
	Pre-MAP (mmHg)	Post-MAP (mmHg)	Pre-HR (bpm)	Post-HR (bpm)	Pre-MAP (mmHg)	Post-MAP (mmHg)	Pre-HR (bpm)	Post-HR (bpm)
1	104.7	92.0	62.0	63.0	113.3	116.0	70.0	70.0
2	95.3	102.0	65.0	68.0	91.3	92.0	68.0	60.0
3	111.3	98.7	66.0	72.0	91.3	89.3	82.0	71.0
4	77.3	89.3	68.0	68.0	98.0	98.7	61.0	60.0
5	90.7	96.7	59.0	67.0	119.3	116.7	71.0	75.0
6	80.0	89.3	55.0	53.0	69.3	73.3	62.0	54.0
7	94.7	92.7	78.0	78.0	90.7	90.7	62.0	66.0
8	120.0	108.7	54.0	65.0	113.3	108.0	57.0	57.0
Mean	99.1	96.1	63.4	66.8	98.3	98.1	66.6	64.1
SD	14.1	6.8	7.8	7.2	16.4	14.7	7.9	7.4

Table 6: ANCOVA calculations for age, MPI, height and weight as cofactors for PWV after WBV. Significance was set at $p \leq 0.05$.

	Age	MPI	Height	Weight
	p value	p value	p value	p value
Aorta	0.40	0.61	0.20	0.20
Leg	0.15	0.81	0.10	0.30
Arm	0.78	0.34	0.72	0.17

Table 7: ANCOVA calculations for HR related cofactors on PWV values after WBV. Significance was set at $p \leq 0.05$.

	Baseline HR	Δ HR after WBV
	p value	p value
Aorta	0.30	0.49
Leg	0.40	0.59
Arm	0.60	0.69

Table 8: ANCOVA calculations for MAP related factors. Significance was set at $p \leq 0.05$.

	Baseline MAP	Δ MAP after WBV
	p value	p value
Aorta	0.17	0.49
Leg	0.90	0.67
Arm	0.38	0.40

Table 9: ANCOVA calculations for changes in HP and MAP co-factored simultaneously. Significance was set at $p \leq 0.05$.

	Δ HR and Δ MAP after WBV
	p value
Aorta	0.37
Leg	0.76
Arm	0.23

Table 10: Pearson's r correlation for age, TPI, height and weight and changes in PWV after WBV for all blood vessels measured. Significance was set at $p \leq 0.05$.

		Age		TPI		Height		Weight	
		r value	p value	r value	p value	r value	p value	r value	p value
Aorta	Δ PWV	-0.44	0.91	0.67	0.06	0.35	0.38	0.08	0.83
Leg	Δ PWV	-0.43	0.28	-0.26	0.52	-0.38	0.92	-0.13	0.74
Arm	Δ PWV	0.39	0.33	-0.15	0.70	0.25	0.54	-0.12	0.76

Table 11: Pearson's r correlation for HR and MAP cofactors and changes in PWV after PS and WBV for all blood vessels measured. Significance was set at $p \leq 0.05$.

		Baseline HR		Δ HR with WBV		Baseline MAP		Δ MAP with WBV	
		r value	p value	r value	p value	r value	p value	r value	p value
Aorta	Δ PWV	0.24	0.55	-0.39	0.33	-0.11	0.79	-0.27	0.50
Leg	Δ PWV	0.28	0.49	0.07	0.86	-0.31	0.44	0.37	0.36
Arm	Δ PWV	-0.54	0.16	-0.23	0.57	0.10	0.80	-0.24	0.56

Table 12: Results of the 2-way and 1-way ANOVAs for each vessel measured. *denotes significant change ($p < 0.05$).

	2-way ANOVA	1-way ANOVA	
	P value	PS (p-value; ES)	WBV (p-value; ES)
Aorta	0.64	0.731; 0.11	0.117; 0.12
Leg	0.801	0.047*; -0.39	0.111; -0.27
Arm	0.918	0.206; -0.19	0.279; -0.25

Table 13: Results of the 2-way ANOVA comparing pre- and post- PWV values for the severity and level of injury groups. Significance was set at $p < 0.05$. ** denotes trend ($0.05 < p < 0.10$)

	Severity		Level	
	Complete	Incomplete	Above T5	Below T5
	2-way ANOVA (PS vs WBV)	2-way ANOVA (PS vs WBV)	2-way ANOVA (PS vs WBV)	2-way ANOVA (PS vs WBV)
	p value	p value	p value	p value
Aorta	0.669	0.936	0.165	0.138
Leg	0.665	0.204	0.502	0.061**
Arm	0.911	0.207	0.971	0.913

Appendix E: Visual Representations of the Apparatus



Figure 29: Picture of the WAVE equipment, platform and standing frame.

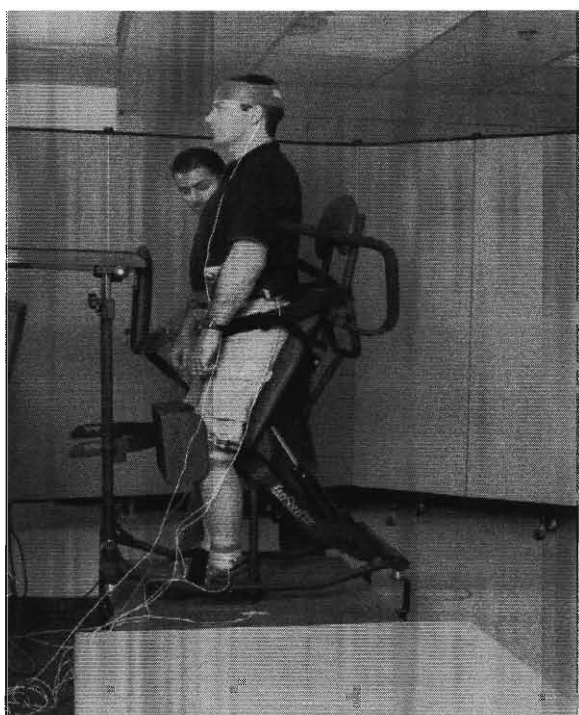


Figure 30: Visual representation of how the participant stood on the vibration platform.